MALARIA AT HOME AND ABROAD

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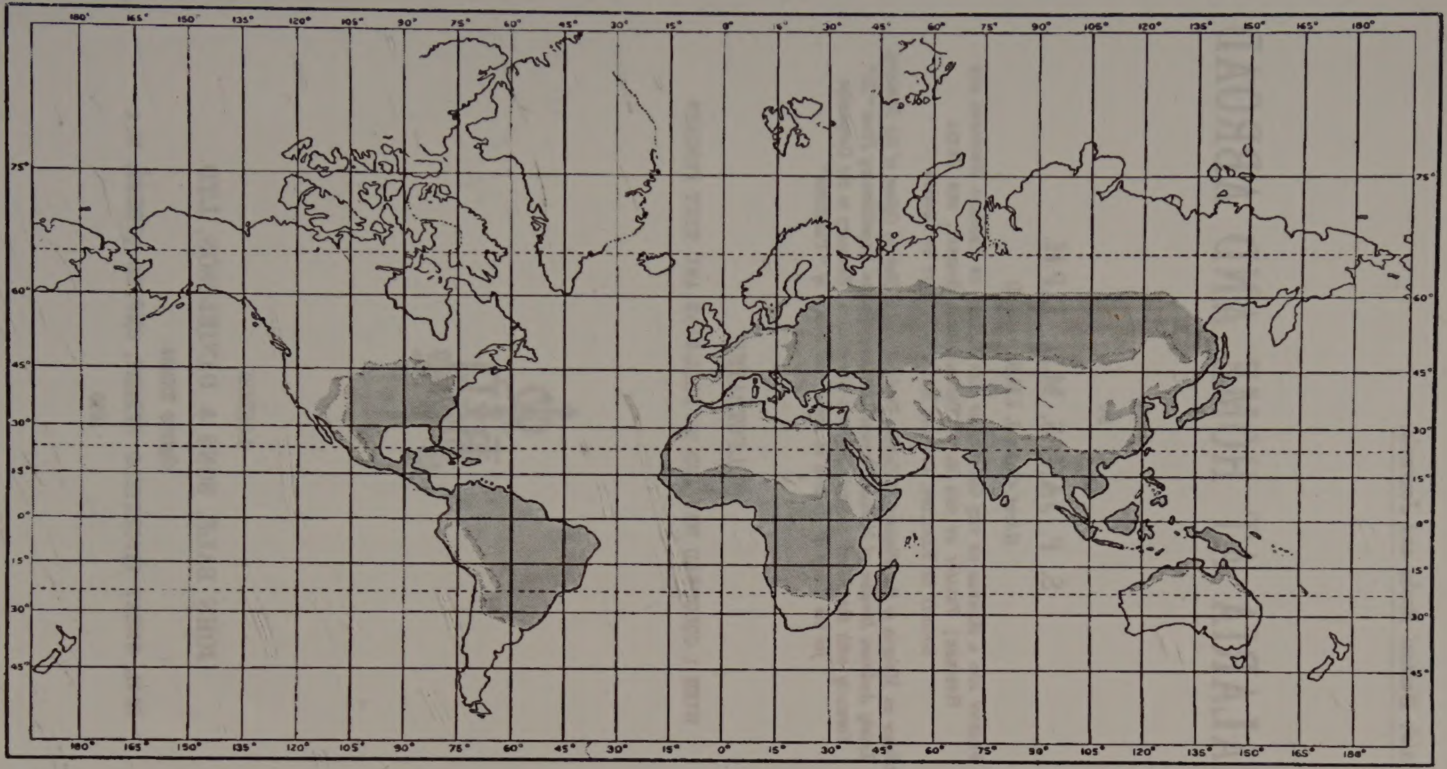

THE PRESENT DISTRIBUTION OF MALARIA.

Bale's Medical Books and Journals.

MALARIA AT HOME AND ABROAD

BY

S. P. JAMES, M.D., D.P.H.

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ILLUSTRATED

WITH 1 COLOURED MAP AND 104 FULL-PAGE AND TEXT FIGURES

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1920

TO

SIR PATRICK MANSON,
G.C.M.G., F.R.S.,

THE FATHER OF MEDICAL RESEARCH IN THE TROPICS

AUTHOR'S EXPLANATORY NOTE.

For some months in 1917 and 1918, under arrangements made by the War Office and the Local Government Board, I held a series of practical classes on malaria, which were attended by Officers of the Royal Army Medical Corps and by civilian Medical Officers of Health. The authorities of the London School of Tropical Medicine courteously provided accommodation and facilities for laboratory work, and Sir Patrick Manson, Colonel Alcock, Dr. Daniels and Dr Leiper generously gave me their personal assistance, which ensured the success of each course of lectures and demonstrations. At the conclusion of the series I summarised the subject-matter of my demonstrations in an article entitled "Practical points in the study of malaria and its diagnosis, treatment, and prevention," which was published by the Local Government Board in No. 119 of their Public Health Reports. The present book is a fuller account of the subjects reviewed in that article, and is intended to be an elementary guide to medical men and administrators who may have to deal with malaria at home or abroad during peace or war.

Readers will note that, in addition to recording the results of my own experience, I have utilised to a considerable extent the writings of other workers in the Indian Medical Service, particularly those of my friend Major S. R. Christophers, whose reputation as an expert malariologist is world-wide. If in any instance I have inadvertently omitted to state the source of the information recorded, I hope that the workers concerned will regard this reference as an acknowledgment of my indebtedness.

After the proofs had been passed for printing, I asked Sir Patrick Manson if he would write a "foreword" to speed the book on its mission. He permits me to give the following extract from his reply: "I have kept your book long, but it is a big affair which does not admit of skipping. I have read it from *alpha* to *omega*, and can conscientiously say that it is a fine performance which is bound to do an immense amount of good. The book requires no foreword from me or anyone else: it speaks for itself."

I know no man so "bénigne" as Sir Patrick.[1] His generous appreciation prompts me at once to tell the reader that the book does not pretend to be a complete treatise; it is by no means free from omissions, some premeditated, others unintentional. Sir Patrick himself very kindly filled in some of these gaps by suggesting: (1) that greater emphasis might be laid on the importance of suspecting malaria in children, particularly when nervous symptoms, fits, languor, &c., are present; (2) that for children with stuporose or comatose symptoms, treatment by repeated enemata of quinine is of proved value; (3) that in adults the symptoms of aphasia, paresis of eye muscles, quinine amblyopia and malarial amblyopia might receive more notice; (4) that the tropical practitioner should always carry in his bag a box of slides and, if he has to go some distance from his laboratory, a small travelling microscope for immediate use. "No man has a right to practise in malarial countries, or as a consultant in this country, who cannot use his microscope in the diagnosis of malaria and other blood parasites."

---

[1] See the dedication in Colonel Alcock's "Entomology for Medical Officers," 2nd Edition, 1920.

I have endeavoured to make good use of these and other practical suggestions which I have received.

8, *Symons Street,*
Sloane Square, S.W. 3.
April, 1920.

S. P. James.

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MALARIA AT HOME AND ABROAD.

CHAPTER I.

I.—Definition of Malaria.

MALARIA in man is the disease caused by the specific pathogenic organism ordinarily known as "the human malaria parasite." The disease in its typical form is characterized clinically by the regular recurrence of paroxysms of fever at definite intervals of twenty-four, forty-eight, or seventy-two hours. These attacks of fever, if recognized at a sufficiently early stage, always yield to proper treatment by quinine (fig. 1). In nature the disease is spread in only one way, namely, by the agency of a particular kind of mosquito.

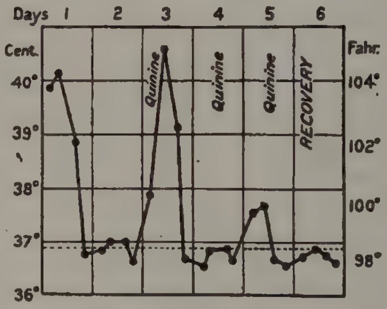


FIG. 1.

II.—A General Description of the Specific Pathogenic Agent.

The human malaria parasite is an animal of a primitive type belonging to the lowest division of the animal kingdom, namely, the PROTOZOA. Its chief characters may be described in a general way as follows:—

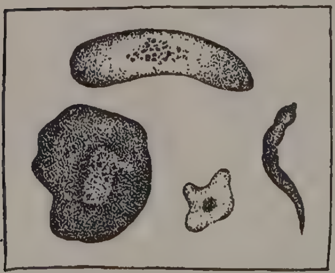


FIG. 2.

(1) The entire individual, in whatever form it may appear, is composed of only one cell, which is a microscopic mass of protoplasm containing a nucleus (fig. 2).

(2) It has no definite organs for locomotion or for ingesting food; but its body protoplasm is "irritable," moves by amœboid activity, assimilates nutriment, grows and divides,

and produces by chemical processes a variety of chemical compounds, some of which cause the fever from which an infected person suffers.

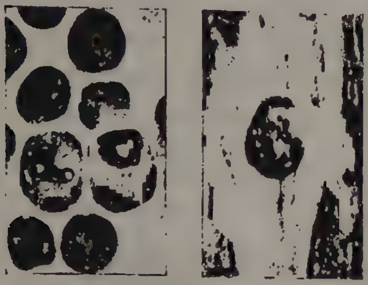

A B

FIG. 3.

(*Photographed by Dr. A. Norman.*)

(3) It is always an intracellular parasite of another organism at whose expense it lives, and which for this reason is called its host. Like some other lowly animals the malaria parasite passes its life in two hosts: one of them is man, the other is a particular kind of mosquito. In man it is parasitic in the red blood corpuscles (fig. 3, A); in the mosquito it is parasitic in the tissues of the stomach wall (fig. 3, B) and in the salivary glands.

(4) It has two modes of reproduction, asexual and sexual. The asexual method consists simply in the division of a full-grown parasite into a number of smaller ones. This method of multiplication occurs while the organism is parasitic in the red blood corpuscles of man (fig. 4). The sexual method consists first in the development of forms which have acquired different properties, namely, male and female (fig. 5). These forms arise while the parasite is in the blood of man, but they remain quiescent in the red corpuscles until the particular kind of mosquito which is the second host sucks them into its stomach with the blood which it extracts when feeding upon a patient. In the stomach of the mosquito the male parasite extrudes processes which function as spermatozoa and fertilize the female parasite, which afterwards, by a complicated process of growth and division, develops within its body a great number of young forms which, when reintroduced (by the bite of the mosquito) into the blood of man, enter the red corpuscles and become young parasites exactly similar to the original ones.

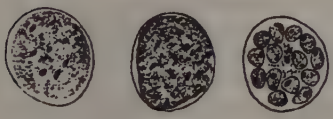


FIG. 4.

(*After Manson.*)

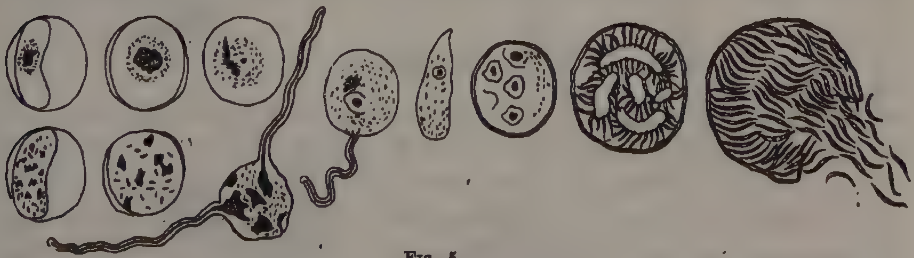


FIG. 5.

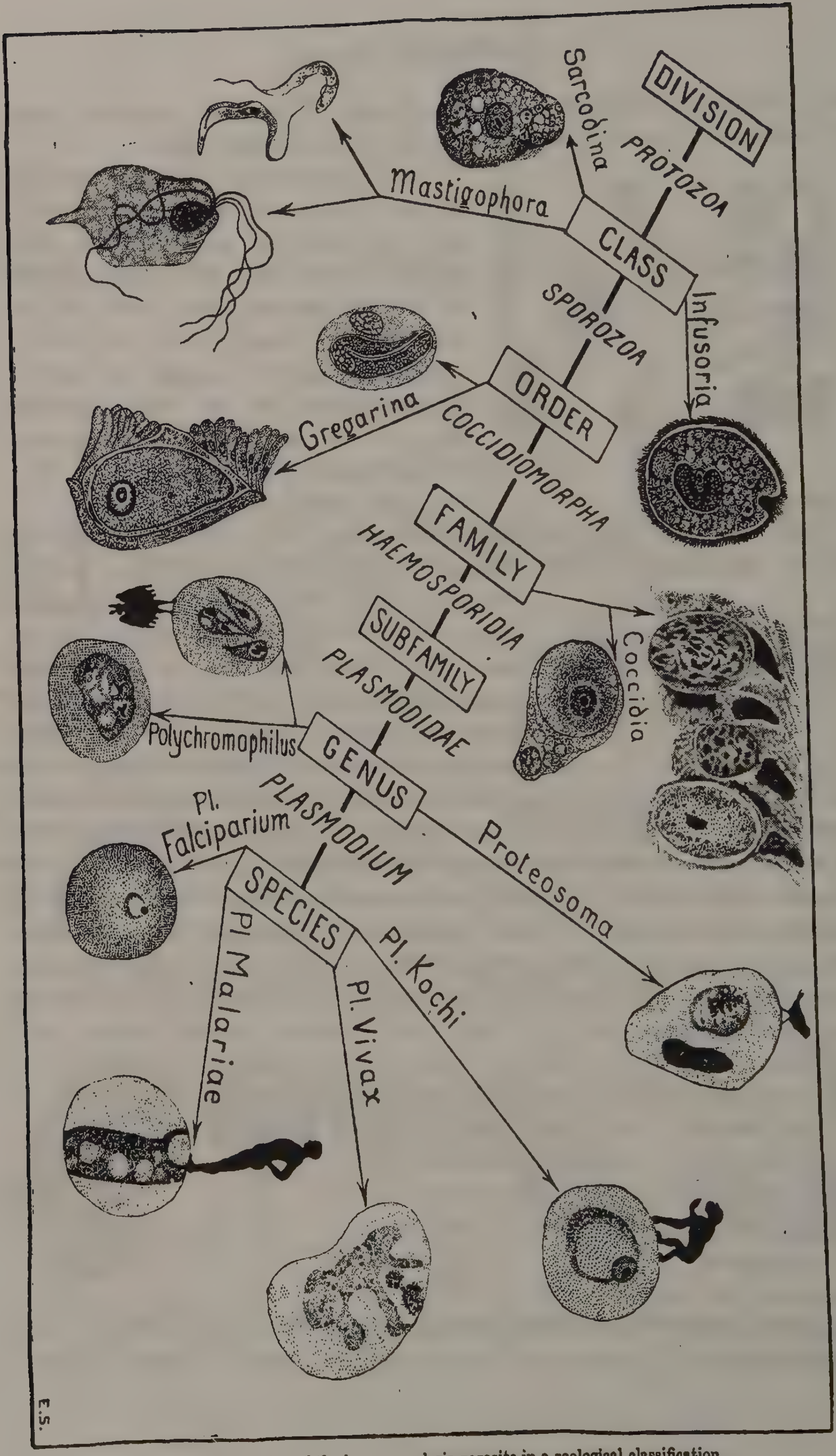
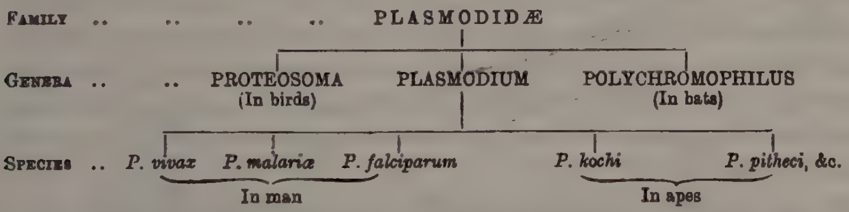


Fig. 6.—The position of the human malaria parasite in a zoological classification.

(5) Three distinct morphological types of the parasite are recognized, and they differ from one another to a degree which justifies the view that they are separate species. It happens also that each of them gives rise to a specific type of malarial fever. The following are the names usually given to these different species of the parasite and types of the fever.

Usual names of the parasite	Generic and specific name	Usual names of the fever
(1) The simple tertian parasite, *or* The benign tertian parasite, *or* The tertian parasite	*Plasmodium vivax* (Grassi and Feletti)	Simple tertian fever, *or* Benign tertian fever, *or* Ordinary tertian fever, *or* Tertian fever
(2) The quartan parasite	*Plasmodium malariæ* (Laveran)	Quartan fever
(3) The malignant tertian parasite, *or* The æstivo-autumnal parasite, *or* The tropical parasite, *or* The pernicious parasite	*Plasmodium falciparum* (Welch; Blanchard), *or* *Plasmodium præcox* (Doflein), *or* *Laverania malariæ* (Grassi and Feletti)	Malignant tertian fever, *or* Subtertian fever, *or* Æstivo-autumnal fever, *or* Pernicious tertian fever

(6) The parasite, in several of the forms which it assumes in human blood and in the tissues of the mosquito, resembles certain blood parasites with which some mammals and birds are affected; but it differs from them—and they differ from one another—in characters which are of generic or specific value. In zoological classifications it is usual to group these parasites and the three species of the human malaria parasite in a *family* termed the PLASMODIDÆ as follows:—



(7) The position of the human malaria parasite in relation to other protozoa, as given in zoological systems of classification, is shown diagrammatically in fig. 6.

III.—The Life-History of the Parasite.

On the above characters, and with the aid of fig. 7 (p. 6), we may now describe the life-history of the human parasite. It has already been indicated that the whole life of the parasite is passed in two hosts, namely, man and a particular kind of mosquito, and that even in those hosts it would quickly die if it were not protected within blood or tissue cells from which it obtains nutriment. For the sake of simplicity we may commence the life-story with the young form of the parasite as it is found in one of the red corpuscles of a man's blood (fig. 7, No. 1). In the living state it appears, when examined under a microscope, as a small unicellular mass of protoplasm occupying only a small portion of the corpuscle and undergoing slow amœboid movement. In dead specimens which have been appropriately stained a nucleus and a small vacuole-like area can be distinguished. At this stage it is termed a *trophozoite.* It grows by assimilating the corpuscular hæmoglobin, the waste products of which remain in the body protoplasm of the parasite, and can be plainly seen as dark brown granules or rods which are variously called "malaria pigment" or "melanin" or "hæmozoin." Some of these are indicated in Nos. 2 and 3 of fig. 7. When the parasite has grown to its full size so that it nearly fills its corpuscle it is termed a *schizont,* and a little later the vacuole-like area disappears, amœbid movement ceases, the grains of waste matter ("malaria pigment") become collected in a mass, and the nucleus and body protoplasm of the parasite divide up into a number of small parts, called *merozoites* (fig. 7, Nos. 5 and 6), each of which will become a new parasite exactly like the original one. These parts or "segments" remain in contact with one another for a short time, and it is at this stage that the appearance under a microscope is often described as being "like a daisy" or "like a rosette." Then they burst from the red blood corpuscle and quickly attach themselves to neighbouring uninfected corpuscles which they contrive to enter. In them they grow in the same manner as the original parasite did, ultimately reaching their full size and dividing into a number of embryo parasites which again enter other corpuscles and go through the same cycle. This is the asexual method of multiplication (*schizogony*) by simple division of a full-grown parasite (*schizont*) into a number of parts (*merozoites*), each of which becomes a young growing parasite (*trophozoite*) like the original one; and it will be clear that, even if at the beginning of the story only one corpuscle contained a parasite, a very large number will by this method soon become infected.

After this method of multiplication has gone on for a few days some of the young parasites, instead of proceeding to develop in the above manner acquire sexual properties and become what are called *gametocytes*—some of them being male (*microgametocytes*), others female (*macrogametocytes*). (See fig. 7, Nos. 7 to 10.) Even at a comparatively early stage of their development they differ from the asexual *schizonts* in having no vacuole-like area, in presenting little or no amœboid movement, in appearing globular and more solid, and in containing more pigment. When full-grown they appear as coarsely pigmented round or crescent-shaped bodies enclosed within the thin envelope of the red blood corpuscle and with a nucleus which shows no sign of division (10). In the blood of man they undergo no further development, and it is therefore at this stage of the life-history of the parasite that a second host becomes necessary. Such a host is a mosquito of the sub-family or group called the *Anophelinæ.* When a mosquito of this kind bites a person with these sexual forms of the parasite in his blood some of them are carried into the mosquito's

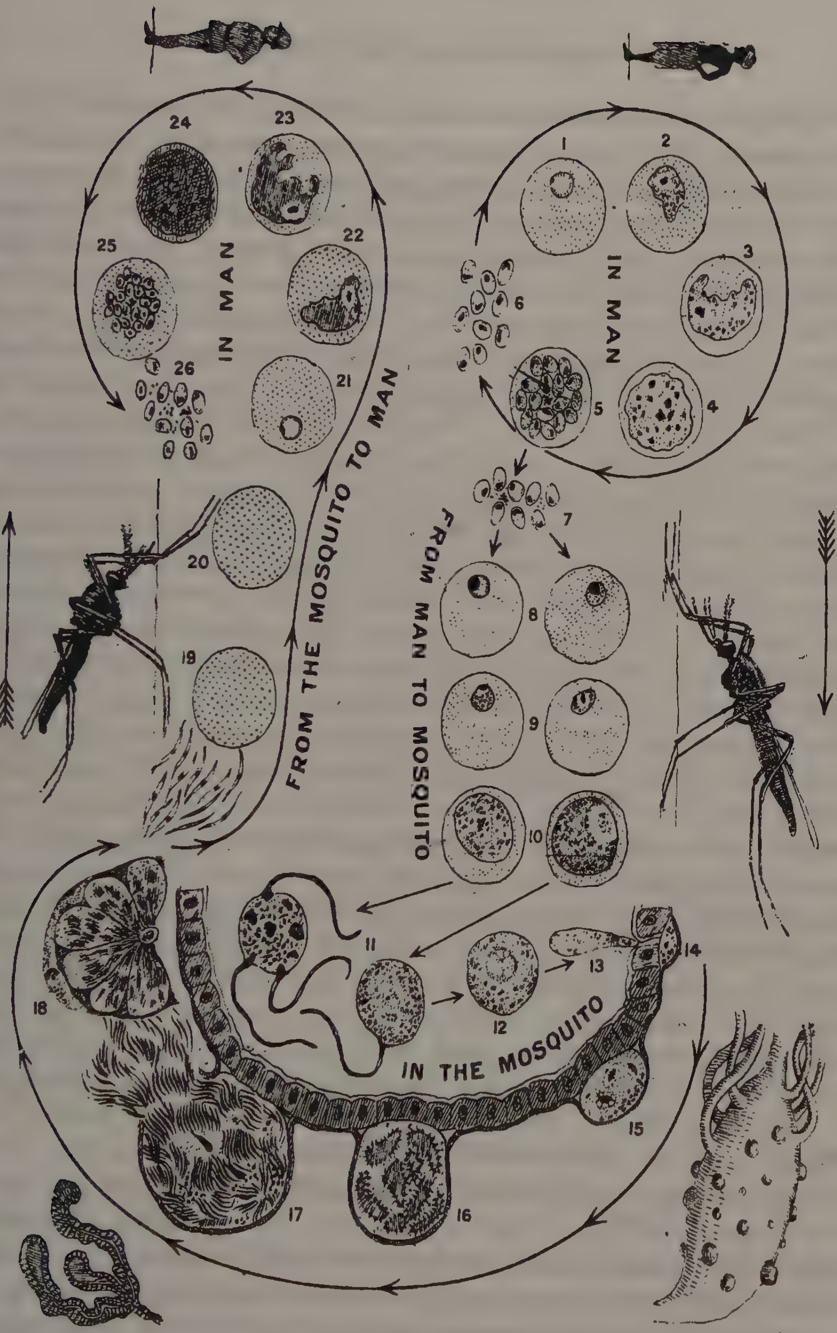


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Fig. 7.—Cycle of the benign tertian malaria parasite (*P. vivax*) in man and in the mosquito.

stomach with the blood which the insect extracts, and there they undergo the following development: First the male and female parasites escape from the red blood corpuscles and are free in the fluid in the mosquito's stomach. Then the parasites throw off the effete vegetative portions of their nuclear chromatin and become sexually ripe for fecundation. At this stage they are termed *gametes*. The female form assumes a spherical shape and granular appearance; the male form extrudes three or four long filaments (*microgametes*, sometimes incorrectly called "flagella") which, after lashing about for a few moments, break away from the body of the parasite and swim about in the fluid in the mosquito's stomach (fig. 7, No. 11). They are the true male element in the sexual process. When one of them comes in contact with a female parasite it penetrates into it and fertilizes the true female element (*macrògamete*) contained in it (fig. 7, Nos. 11 and 12.) After this act of fertilization the female parasite acquires new characters and is termed an *oökinet*. Changing from the shape of a sphere to that of an ovoid with a pointed end (fig. 7, No. 13) it begins to move about ("*travelling vermicule*") and, making for the inner wall of the stomach of the mosquito, it passes through the internal coats and comes to rest between the epithelial and muscular layers. After being surrounded by a thin cyst-wall it becomes an *oöcyst* (ordinarily called a "zygote") and begins to absorb nutriment from the host and to grow until it attains a comparatively large size (fig. 7, Nos. 14, 15). By a process of nuclear and protoplasmic division and subdivision (called *sporogony*) there are formed in the oöcyst irregularly shaped masses called *sporoblasts* (No. 16), from which particles of nuclear chromatin pass to the periphery and become the nuclei of embryo parasites called *sporozoites*, of which an immense number ultimately fill the full-grown oöcyst. Each is a tiny motile ribbon of protoplasm, sharper pointed at one end than at the other, and having a centrally placed nucleus. The oöcysts ("zygotes") which contain them project through the wall of the mosquito's stomach into the lymph sinuses which surround it, and when they are fully formed the wall of the oöcyst bursts, and they are liberated into these lymph sinuses, which are part of the general circulating system of the mosquito (fig. 7, No. 17). They are conveyed in the circulation to various parts of the mosquito's body, but chiefly towards the head and the salivary glands. When they reach the latter they penetrate the outer wall of the gland cells and come to rest in them (fig. 7, No. 18) and in the salivary duct which has its external opening at the point of one of the piercing stylets of the proboscis which enter the skin in the act of biting. Each time this mosquito bites a person it injects some of the sporozoites into his blood with the salivary fluid. In the blood of man the sporozoites penetrate into the red corpuscles (fig. 7, Nos. 19, 20, 21), and are found as young "ring" forms of the parasite identical with those from which the description of the life-story was commenced.

MODE OF SPREAD OF MALARIA.

From what has been described above it will readily be seen how malaria is contracted and spread. An *anopheline* mosquito bites a person who has been suffering from malaria and has sexual forms of the parasite in his peripheral blood. These sexual forms are taken into the mosquito's stomach with the blood which it sucks in, and there they undergo the development just described, resulting in the formation of numerous sporozoites which become lodged in the salivary or poison gland of the mosquito. When this mosquito next bites anyone, it injects some of the sporozoites into his blood and so produces a malarial infection in him similar to that of the patient from whom it originally sucked blood.

Fortunately not every kind of mosquito can act as a suitable host for the human malaria parasite, and experiments have shown that in all probability mosquitoes of only one kind—namely *anopheline* mosquitoes—can so act. Also malaria cannot be contracted, even by the bite of an *anopheline,* unless that mosquito has sporozoites in its salivary glands. This means first that it must have bitten a malaria-infected person at least ten days previously (for, under the most favourable conditions, this is the shortest time required for the complete development of the parasite in a mosquito); second, that the patient, when he was bitten, must have had mature sexual forms of the parasite in his peripheral blood; third, that the temperature and other factors necessary for the development of the parasite in the mosquito's body were favourable.

A malarious place is one in which these and other necessary conditions are frequently fulfilled. In such places it is always possible, by examining the inhabitants, to find that a considerable number have sexual forms of the parasite in their blood, and it is always possible, by dissecting several hundred anophelines caught in dwelling houses during the malarious season, to find that a certain number have sporozoites in their salivary glands.

The factors concerned in bringing about a malarious condition of this kind will be considered more fully in the next chapter.

SUMMARY OF THIS CHAPTER.

We may briefly recapitulate here the chief observations and conclusions recorded in the foregoing pages:—

(1) Human malaria is caused by infection with a minute parasitic animal belonging to the lowest grade of the animal kingdom, the PROTOZOA. Three separate morphological types or species of the parasite are recognized and each of them gives rise to a distinctive type of malarial fever: namely *Plasmodium vivax* which causes benign tertian fever, *P. malariæ* which causes quartan fever, and *P. falciparum* which causes malignant tertian fever.

(2) The parasite passes its life in two hosts, namely man and *anopheline* mosquitoes.

(3) In man it multiplies by a simple process of division (*schizogony*) for some days and then develops sexual forms (*gametocytes*) which for their further development require to be taken into the body of the second host, which is an *anopheline* mosquito.

(4) This is effected when such a mosquito bites a man with those forms in his blood.

(5) In the mosquito's body the sexually mature female form (*macrogamete*) is fertilized by the male (*microgamete*) and the cell which results comes to rest in the stomach wall of the mosquito, develops a thin covering, and becomes an oöcyst. By the growth and division of the öocyst an enormous number of new forms of the parasite, called *sporozoites*, are produced, and they become lodged in the salivary gland and duct of the mosquito.

(6) When this mosquito next bites a person some of the sporozoites are injected into him with the salivary fluid.

(7) In his body they develop in the red blood cells into young parasitic animals exactly similar to the original ones.

(8) As the parasite does not pass any part of its life in any other environment than men and mosquitoes, it follows that men and mosquitoes are the only sources of malarial infection; and it has been proved almost beyond any possible doubt, that there is no other method by which malaria is contracted in nature than by the bite of an infected *anopheline* mosquito.

(9) Malaria cannot be contracted from drinking impure water, or from the soil, or by breathing impure air; and water and air are only indirectly connected with malarial infection in the sense that they are the home of malaria-carrying mosquitoes.

CHAPTER II.

Factors concerned in the Spread of Malaria.

A knowledge of the etiological cycle which was described in the last chapter enables us to investigate, in the laboratory and in the field, the various factors which are concerned in the occurrence, spread, distribution, and intensity of malaria. In the accompanying diagram (fig. 8) these factors are represented figuratively by the links of the three chainlets which are connected together to represent the etiological chain. The chain may be broken either at one of the large links which join the chainlets or at any of the smaller links. These are figured of different sizes and shapes to indicate that they stand for various circumstances and conditions of which not all are of equal influence. We are still very far from having a sufficient knowledge of all these circumstances and conditions, and their study, especially by methods which aim at obtaining "quantitative" results, offers the best hope of improving the present practice of malaria control.

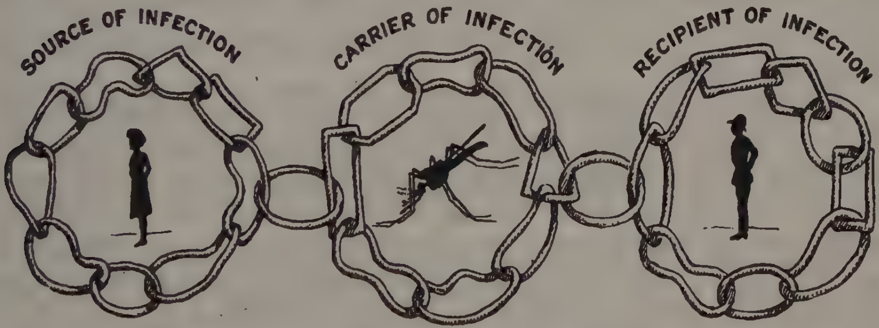

Fig. 8.—The etiological chain.

It is not intended here to do more than summarize briefly some of the chief points.

(1) Factors relating to the Source of Infection.

In nature the source of malarial infection is always a human being who has in his peripheral blood the sexually differentiated forms of the parasite (*gametocytes*) which alone are capable of spreading the disease. In a malarious locality such gametocyte carriers must be sought among both the indigenous and the immigrant population. Some of them may be actually suffering from an attack of fever, others may be going about their usual occupation without any symptoms of illness ("HEALTHY MALARIA CARRIERS"). In the tropics it is usual to find in very malarious places that the young children of the indigenous population are the chief sources of infection. In less malarious places carriers are distributed more evenly among people of different ages, and are found commonly among adults. In Europe at the present time the sources of infection include many cases of imported malaria among soldiers who have returned from the Balkans and other Eastern war areas.

Circumstances which influence the number of malaria carriers in a locality are therefore very important factors in connection with the spread of the disease. They are not more important, however, than are various circumstances relating to the actual parasites (*gametocytes*) which these persons carry in their blood. In a first attack of malaria these gametocytes appear in the peripheral blood about a week after the onset of definite attacks of fever, and they attain their greatest number about ten days after the asexual parasites have become most numerous. The *sex*, *age* and *number* of these gametocytes are of great importance in relation to the spread of the disease.

As regards *sex* it is necessary, in order to ensure the infection of anophelines, that both male and female gametocytes shall be present in about equal numbers in the blood of the patient. Sometimes it happens that no male forms can be found among the gametocytes present in the blood of a malaria carrier. Grassi and others have reported complete failure to convey the disease by anophelines fed upon such patients, and it has been suggested that in certain circumstances the spread of malaria might best be stayed by measures for breaking the chain of infection at this essential, but relatively weak, link.

As regards *age* it is well known that when gametocytes first appear in the peripheral blood they are immature and non-infective to anophelines. Possibly the sexual forms occupy from a week to ten days in growing from the youngest stage to the degree of maturity at which they are capable of developing in the mosquito.

As regards *number* we know that even under favourable conditions only a small proportion of the gametocytes which an anopheline sucks into its stomach contrive to continue their development in its tissues. Experiments made by Darling in Panama indicated that a patient whose blood contains fewer than twelve gametocytes per cubic millimetre of blood is not infective to mosquitoes: and from a notable series of experiments made by Christophers in India it may be inferred that even only one mosquito which has fed upon a heavily infested carrier may cause more malaria than many mosquitoes which have fed upon scantily infested carriers. If this is true it must be the case that the actual number of malaria carriers in a place is of less importance than is the number of heavily infested carriers. Indeed, there is evidence that the presence of such heavily infested carriers is essential to the occurrence of malaria in epidemic form.

Unfortunately we know almost nothing of the influences which tend to increase the gametocyte output in individual cases or to cause an unusual increase in the number of heavy gametocyte carriers in a particular community.

The *species of parasite* concerned is also a factor to be noted in connection with this subject. The malignant tertian parasite (*P. falciparum*) produces, as a rule, more gametocytes than the other species. But the benign tertian parasite (*P. vivax*) causes more frequent relapses with the appearance of gametocytes in the peripheral blood, and it may therefore have more opportunities of spread. The parasite of quartan fever (*P. malariæ*) produces, as a rule, fewer gametocytes than either of the other two species, but it persists for a longer time in the human host, and is therefore sometimes present in localities which have become free from the other species.

(2) FACTORS RELATING TO THE CARRIER OF INFECTION.

It has already been stated that in nature malaria is carried from person to person by female mosquitoes belonging to the subfamily *Anophelinæ*, which alone are capable of acting as insect hosts of the human malaria parasite. In this connection the factors which influence the spread of the disease relate to the particular species, habits, and numerical prevalence of the anopheline concerned and to the circumstances which promote or retard the development of the parasite in its tissues.

Species.—Although probably all species of anopheline mosquitoes can be infected with malaria under favourable conditions in the laboratory, not all become infected to the same degree; and it has been found by field research that in nature some species are much more concerned with the spread of the disease than others. Stephens and Christophers were the first to make this important observation, and their results have been confirmed by many workers. For example, Bentley in Bombay collected at the same time from the same houses 837 specimens of *Anopheles stephensi* and 772 specimens of *A. rossii*. He carefully examined the stomachs for oöcysts and the salivary glands for sporozoites with the following results:—

Species of mosquito	Number dissected	Percentage with oöcysts in the midgut	Percentage with sporozoites in the salivary glands
A. stephensi	837	10·0	3·5
A. rossi	772	0·0	0·0

These observations showed that *A. rossii* played no part in the spread of malaria in Bombay. In the same way *A. pulcherrimus* has been shown not to be actively concerned in spreading malaria in Mesopotamia, and *A. pharoensis* not to be much concerned with its spread in Egypt. On the other hand, some examples of species which have been proved to be active propagators of the disease under natural conditions are: in Europe, *A. maculipennis;* in Asia, *A. culicifacies;* in Africa, *A. funestus;* and in America, *A. albimanus.*[1]

Habits.—A "domestic" anopheline, like *A. maculipennis*, which frequents and remains in dwelling houses, has more influence on the spread of malaria than a species like *A. bifurcatus*, which spends most of its life in the open. Again a species which passes the winter in the adult stage (as does *maculipennis*) may carry sporozoites in its salivary glands, and may infect people throughout that period. This cannot happen in regard to a species like *bifurcatus*, of which all the adult insects die at the onset of winter. Various species differ from one another also in their zone of flight, length of life, food supply, and other habits which affect their relative importance in spreading malaria.

In regard to *numerical prevalence* observations must be made on the particular species which is carrying malaria at the time rather than on all anophelines which may be present in the locality. In some malarious areas in India there are as many as fourteen species of anopheline mosquitoes of which only one or two may be actively concerned in spreading the disease. "Quantitative" results which show the influence of the numerical abundance of an infecting species are almost entirely lacking. The study of this subject is complicated by the well-established observation that an infecting anopheline not only feeds regularly for a number of nights, and so may infect many people, but often feeds upon several persons during a single night. From this observation it follows that in certain circumstances only a very few anophelines are sufficient to cause a considerable spread of malaria. Instances in which this has happened are sometimes found during field work. Thus at Ennur, in Madras, where most of the inhabitants suffered from malaria, the infecting species of anopheline was so rare that three experienced observers were occupied for several days in catching about sixty specimens. On the other hand, there are places in which numerous anophelines of a species which is an efficient carrier are associated with little or no malaria. Such examples show that the numerical prevalence of anophelines is only one of many factors which influence the spread of malaria, and that it is by no means always the most important factor. Indeed, the amount of malaria in a locality will vary in accordance with variations in the number of anophelines only when all the other factors remain equal and constant. In some localities in England from which malaria has disappeared, anopheline mosquitoes are still as prevalent as in many very malarious places in the tropics. This shows that in England the factor of numerical prevalence of anophelines was of less importance than were some other factors which were concerned in the former spread of the disease.

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[1] A list of proved malaria-carrying species will be found on p. 60.

Of the circumstances and conditions which promote or retard the development of the parasite in the mosquito *temperature* is the most important. At a constant temperature of 77° F. the benign tertian parasite completes its development in *A. maculipennis* in eleven days, and at temperatures varying between 59° and 73·5° F. (with an average of 62·5° to 68°) in fifteen days (Roubaud). According to Jancso the lowest temperatures at which the benign tertian parasite will develop in the mosquito are between 59° and 62·5° F., but at those temperatures the period required for the completion of the cycle was found to be fifty-three days. Wenyon found in the Balkans that forty days were required for the parasite to attain maturity at a temperature of 62° F. At a temperature of 77° F. the malignant tertian parasite develops more slowly than does the benign tertian parasite.

The *humidity of the atmosphere* in which the mosquito lives may also have some influence on the development of the parasite in its tissues. In Bombay it was found by Bentley that anophelines were frequently infected during periods of high atmospheric humidity but not at other times.

The infection of malaria-carrying anophelines in some localities appears to be subject to *seasonal variation* which cannot be explained on the ground of temperature or other known influence. In Bombay the minimum temperature in the coldest season rarely falls below 65° F., and there is only a difference of 11·5° F. between the mean temperature of the warmest and coldest months. Bentley, however, from dissections carried out during each of eighteen months in 1909 and 1910, records the results which are shown in fig. 9.

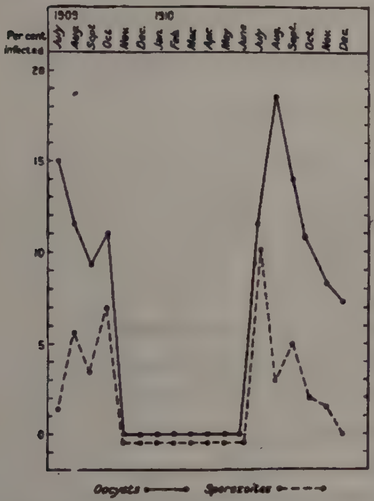

FIG. 9.—Seasonal infection of *Anopheles stephensi* in Bombay, 1909-10.

(3) FACTORS RELATING TO THE RECIPIENT OF INFECTION (SUSCEPTIBLE PERSONS).

Susceptibility is, of course, a factor essential to the spread of malaria. Some races of people, and perhaps some individuals, suffer more from malaria than others in the same environment. The constant introduction of susceptible people into a malarious locality greatly enhances the prevalence and severity of the disease and is sometimes an important factor in the production of epidemics. It is usually called "*the factor of non-immune immigration.*"

Immunity to malaria, when it is present, is almost always a partial immunity acquired by frequent infection and reinfection repeated continuously during a number of years. In a very malarious locality the children of the indigenous inhabitants become infected with malaria when they are a few months old. They suffer all the usual symptoms of the disease and many of them die from it. Those who survive to the age of three or four years will be found to have acquired a considerable degree of *tolerance* to the effects of the parasitic invasion, but parasites will be present in their blood and their spleens will be enlarged often a hand's breadth or more below the ribs. With a continuance of infections and reinfections this tolerance becomes greater, with the result that children of perhaps 8 or 10 years, although still harbouring parasites, may show no symptoms and may be correctly classed as "healthy malaria carriers." Later still they develop in varying degree an immunity to the parasite in addition to being tolerant of its effects, and, when this is so, their spleens decrease in size and parasites can no longer be found in their blood. Fig. 10 shows the result of an examination of the indigenous inhabitants in a malarious place of this kind.

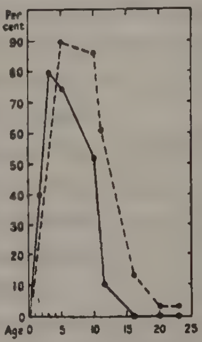

Fig. 10.

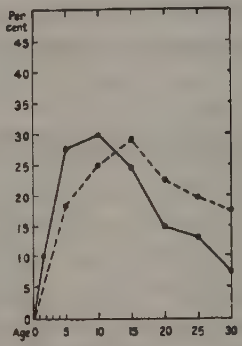

Fig. 11.

In less malarious places, although the stage at which there is tolerance to the effects of infection may be reached at a comparatively early age, many adults will be found to have enlarged spleens and to harbour the parasites in their blood (fig. 11).

Social and Economic Factors.—Christophers has shown very clearly that in malarious localities people of low social status suffer more than those who are well-to-do, and has called attention to the direct and indirect action of various economic factors which influence the spread and intensity of the disease. All the circumstances, for example, which tend to delay recovery,[1] or to lessen the resisting power of individuals, or to increase the amount of exposure to infection, or to bring about close association between the malaria carriers and susceptible persons, enhance the prevalence and severity. Such circumstances often arise in connection with jungle clearing and engineering works in the tropics, and are referred to as "the factor of tropical aggregation of labour." Bentley has described them in the following manner: "In the East the coolie labourers employed on such works are drawn almost entirely from the poorest and most ignorant classes of the population; they are often brought long distances and set down in a country where the climate, and even the food obtainable, differ greatly from that to which they are accustomed. If housed at all they are generally crowded into temporary huts, but frequently they are left to find what shelter they can. Often they have no one to look after them when sick and no means of obtaining food when they are unable to work. Their work is arduous and their pay small; and it is no uncommon thing to find them attempting to exist upon a miserably insufficient diet. Camped, as they usually are, upon the site of the work, their surroundings are almost always highly insanitary and, if much earth-work is going on, the numerous pools of water speedily become the breeding places of countless swarms of mosquitoes. In these circumstances it is not surprising that coolie labourers should be decimated by epidemics. But, whatever happens to the coolies, the work has still to go forward, so that, as long as it is in progress, there is continued immigration of new labourers to fill the gaps caused in the labour force by sickness, desertion, and death. This continual immigration is a further source of mischief, for the constant introduction of gangs of susceptible new-comers into camps which already are hotbeds of disease, increases the trouble just as the addition of fuel to a glowing fire increases the blaze."[1]

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[1] See also the paragraph on the factor of residual infection in Chapter VI, p. 104.

(4) Factors relating to the Environment.

The information given under each of the three headings just dealt with enables us to work out the manner in which various circumstances and conditions in the environment influence the spread of malaria. Some of these factors are: locality and altitude; climate and season; temperature and humidity; winds and calms; rainfall and drought; floods; rivers and irrigation; forest, jungle, desert; fauna and flora in relation to mosquitoes; reclamation and clearing of land; character of the soil and subsoil; opening up and cultivation of the soil; character and abundance of crops; famine and plenty; primitive and civilized conditions; housing and general sanitation; means of communication and other facilities for movement of the population; conditions of peace and of war. Some of these factors act directly on the source, or carrier, or recipient of infection; some act on all of them either directly or indirectly through one or other link in the etiological chain. A factor which by its action on one part of the chain may tend to promote malaria may at the same time by its action on another part tend to lessen the disease. Rainfall tends to anophelism and an increase of malaria, but it brings good crops and prosperity which tend to quicken the recovery rate and lessen the prevalence and severity of the disease. The same factor in one locality may increase malaria while in another it may lessen it (e.g., floods).

It is appropriate to state under this heading what is now considered to be the correct explanation of the serious prevalence of malaria which often follows "opening up the soil." I can best do so by extracting the following paragraphs from a report by Major Christophers. He says: "The belief that severe malaria is often the result of opening up the soil has long been held. To explain this, it has been customary to note that pools are generally formed which are suitable for anophelines to breed in, and that malaria is the result. In reality this is quite an inadequate conception of the true state of affairs. Operations for "opening up the soil" involve certain conditions. The most important is the formation of enormous camps of coolie labourers and their families, drawn from far and wide throughout the district, or even from distant countries. In such camps, of far more importance than extra facilities for the breeding of anophelines, are such conditions as the mixture of races and classes involving aggregation of susceptibles with infected; the depressing effects of hardship, especially affecting the weaker, who in turn, by becoming malarial disseminators take their part in the vicious cycle; crowding of the population into communities larger than occur in ordinary rural conditions, but not large enough to obtain the benefits of urban conditions; and many other factors which need not be specified. Naturally the Europeans and others employed in supervision suffer in the general trouble, since, in their ignorance they dwell in the midst of the natives. The belief that malaria comes from the opening up of the soil is therefore based upon fact, but the responsibility is not with the miasmatic exhalations nor even with the extra facilities for the breeding of anophelines; it is bound up in the general conditions inseparable from the existence of great labour camps in the tropics."[1]

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[1] *Paludism*, No. 2, January 1911, p. 104.

(5) FACTORS RELATING TO THE LINKS WHICH CONNECT THE CHAINLETS.

The spread of malaria depends not only on many factors which influence respectively the source, the carrier, and the recipient of infection, but on other factors which bring the source, the carrier, and the recipient into the necessary close association with one another. In almost any malarious country it is not difficult to find:—

(*a*) Localities in which the presence of many human malaria carriers and numerous anophelines is not accompanied by a corresponding prevalence of new cases.

(*b*) Localities in which only a few malaria carriers and a few anophelines are accompanied by a severe prevalence of new cases.

In instances of the first type there are malarious conditions without much malaria ("Paludism *sine* malaria"); in those of the second type there is much malaria without markedly malarious conditions ("Malaria *sine* paludism"). We cannot in every locality explain such findings completely, but in some the explanation lies in a knowledge of the degree to which there is close association between the human host, the insect carrier, and the susceptible population. By artificial means the links which represent this necessary close association can be cut by taking steps to prevent the insect carrier having access to the particular human beings concerned. In nature the degree of association varies in different localities and circumstances, and, when other factors remain constant, the amount of malaria in the locality varies accordingly. In certain ports on the West Coast of Africa malaria is intensely prevalent and severe among European immigrants, because they live in close association with the indigenous population, who are the chief source of infection. But when in such places Europeans, by chance or design, live at some distance from the native quarter, they largely escape the disease.

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[1] Scientific Memoirs by Medical Officers of the Government of India, New Series, No. 35, 1908, p. 21.

Sometimes careful inquiry is necessary to ascertain the facts in regard to the degree of association. It has happened that non-immune soldiers have lived with malaria-carrying soldiers in a room over a stable in which cows were kept, and have escaped infection throughout a malarious season. In this instance inquiry showed that anopheline mosquitoes were always abundant in the stable, but were seldom or never present in the upper room; and the soldiers expressed surprise that they were never, to their knowledge, bitten. It seemed probable that, from the point of view of the anophelines, the stable presented more suitable and safer resting places than the upper room, and the blood of the cows a more accessible source of food supply than that of the soldiers.

In any particular locality all the circumstances which are represented in our diagram by the links which connect the three chainlets should be ascertained in detail. The above examples are given only to indicate the kind of inquiry which may be necessary.

SUMMARY OF THIS CHAPTER.

We may now recall briefly the chief headings which have been discussed in this chapter.

In describing and explaining the incidence and spread of malaria in any locality, we must inquire into the following subjects, and must endeavour to estimate quantitatively the relative influence of various circumstances and conditions ("factors") relating to (1) the sources of infection; (2) the carriers of infection; (3) the recipients of infection; (4) the environment; (5) the degree of association between 1, 2, and 3.

The sources of infection (Chainlet A) are human beings who harbour gametocytes. In addition to the numerical prevalence of these gametocyte carriers the sex, age, number, and species of the gametocytes which they harbour are important, One heavily infested person may sometimes cause more malaria than several scantily infested persons.

The carriers of infection (Chainlet B) are female anopheline mosquitoes. In regard to these insects, the most important factors are their species, their life-history and habits, and their number; and, in regard to the development of the parasite in their tissues, the most important are temperature, humidity, and season.

The recipients of infection (Chainlet C) are susceptible human beings. Important factors relating to them are relative susceptibility and relative immunity; various social and economic circumstances; habits and customs; housing, &c.

The environment (Chainlet D) figuratively surrounds, and is connected with, all the chainlets *and with each separate link of them.* We have purposely omitted any attempt to represent it in our diagram. Practically all circumstances and conditions which can be named as belonging to the environment have some influence on the spread of malaria. They act partly in a direct manner on the source, the carrier, and the recipient; partly in an indirect manner on various subsidiary factors relating to the development of the parasites in the human and insect hosts. In compiling a list of environmental circumstances and conditions, with a view to ascertain their influence and the mode in which they act, it is helpful to take them in the order of (*a*) those which, so to speak, are "above the earth; (*b*) those which, so to speak, are "on the earth"; and (*c*) those which, so to speak, are "under the earth." Following this plan, we shall not omit to mention under (*a*) such general conditions as light and darkness, sunshine and cloud, &c.; under (*b*) the physiography of the area, the fauna and flora, the food supply and the means of communication; and under (*c*) the porosity and other characters of the soil and subsoil, the level of the subsoil water, the salinity of the natural waters in the locality, their flora, and the enemies of mosquito larvæ which are found in them. We have seen, too, that the mode of action of certain factors in the environment (such as opening up the soil) has sometimes to be sought along unexpected lines.

The factors relating to the connecting links between the source, the carrier, and the recipient are (*a*) those which promote close and continuous association such as the aggregation of malaria carriers and susceptible persons in the same hut or house which is a favourable resort for anophelines; (*b*) those which prevent this association, such as the segregation of non-immunes at some distance from the indigenous population, or the isolation of malaria carriers.

CHAPTER III.

The Practical Work necessary for Field Inquiry into Malaria.

We cannot proceed further with our study of malaria until we have a practical knowledge of the methods employed in carrying out a field inquiry into the disease. I shall therefore devote several chapters to that subject, which is of great importance and interest. The present chapter will deal with the study of the parasite in the human and insect hosts.

HOW TO FIND AND STUDY THE PARASITE IN THE HUMAN HOST.

For finding and studying the parasite in human blood no directions that can be given on paper are of value as compared with the usefulness of practical demonstrations by one who is familiar with the necessary technique. Therefore anyone who wishes to study malaria seriously should endeavour to obtain such demonstrations whenever an opportunity presents itself. In the meantime it is hoped that the following directions and notes may be of service. They are purposely recorded very briefly, and in abrupt, didactic form.

(a) *Taking the Specimen of Blood.*

(1) For a microscopic examination to ascertain the presence of malaria parasites, the blood can be mounted on glass slides either in the fluid state (unstained) or it can be dried and stained. Fluid, so-called "fresh," specimens are invaluable for studying the parasites, but nowadays they are never used for routine diagnostic work. For this reason the method of preparing and examining them will not be described here.

(2) To prepare dried blood films the only articles required are microscope glass slides, and a long straight surgical needle (preferably with the eye snipped off). Good films cannot be made unless the slides, needle, and the patient's finger are clean, quite free from grease, and *thoroughly dry*. The details of making a film are as follows:—

Polish the slide with a silk handkerchief. Clean the pad of the patient's finger-tip and thoroughly dry it. Prick it without hesitation, sharply but not deeply. Lay the needle down on the edge of the table so that it can be quickly picked up again. Rub off the drop of blood that has exuded from the pricked finger. Pick up the slide between the finger and thumb of your right hand, and then with your left hand press out a second drop of blood. Lower the slide so that the drop, as it exudes, will be received on the slide about an inch from one end. Release the patient, and, turning the slide over, take it between the finger and thumb of your left hand. Pick up the needle by its pointed end, and lay its shaft across the slide on, and in, the drop of blood, which will run along the needle. Press the shaft flat on the face of the slide and sweep it evenly along the whole length of the slide (fig. 12). Wave the slide in the air so that the blood film may dry as rapidly as possible. When it is perfectly dry (not before) wrap it in a piece of paper on which all the particulars of the case are written.

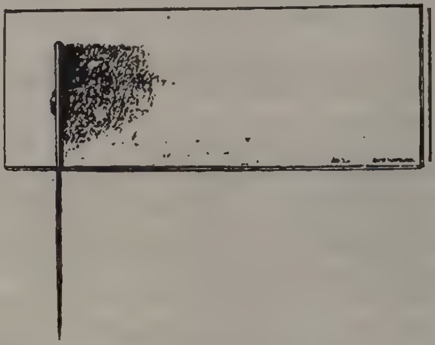

FIG. 12.

The procedure of receiving the drop of blood on the slide, turning the slide over, taking hold of it with the left hand, picking up the needle, laying its shaft flat on the face of the slide, and sweeping the needle over the face of the slide, should be performed rapidly, but steadily. The method is simple, but requires practice.

(3) The naked-eye characters of a good film made in this way are :—

(*a*) The film should occupy the middle area of the slide and should be about two-thirds the length of the slide.

(*b*) The distal end of the film should consist of "tails" or "tags" about half an inch from the end of the slide. This is obtained by using a blood-drop of the correct size.

(*c*) At least one edge of the film should be quite straight, and at a little distance from, and parallel with, the edge of the glass slide.

(*d*) The film should not appear too thick nor too thin. This is a problem of pressing the needle less or more lightly on the face of the slide when spreading the blood. If a patient is very anæmic, use less pressure.

(4) Instead of spreading the drop with a needle it may be spread with the end of a slide in the manner shown in fig. 13. The slide used for this purpose should be of the best quality with ground edges and the corners should be snipped off. Other methods of taking films will be described in the chapter on the diagnosis of malaria.

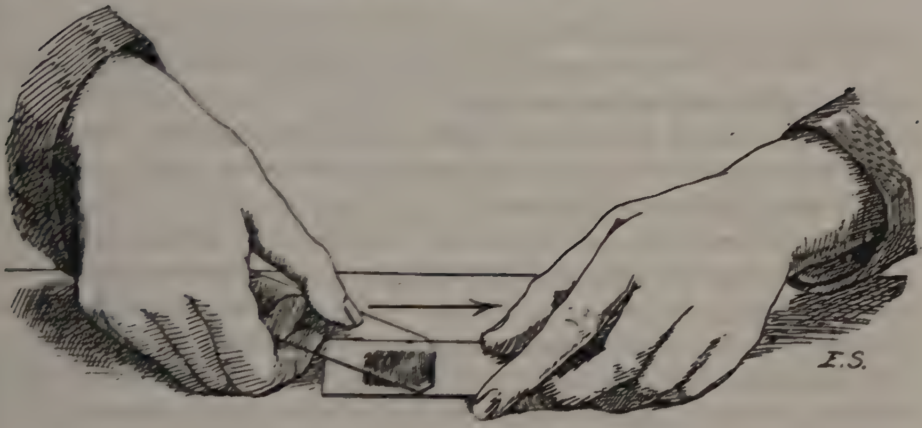

FIG. 13.

(b) Staining the Specimen.

Freshly prepared Leishman's stain is best for the routine diagnostic examination of blood films for malaria parasites. It is a triple stain consisting of a combination of a particular kind of eosin and a particular kind of methylene blue.

(1) Make up some Leishman's stain by dissolving 0·15 gramme of the powder (or one "tabloid," if the stain has been obtained in that form) in 10 c.c. of pure methyl alcohol (free from acetone). Keep the stain in a drop-bottle, do not filter it, and never make up more than will be sufficient for a week.

(2) In a second drop-bottle keep some pure, distilled, water.

(3) In using the stain previous fixation of the dried blood film is not necessary.

(4) Lay the slide (blood film upwards) across two pencils or glass rods placed on a table or over a sink. Hold the mouth of the drop-bottle that contains the stain very near the film and drop sufficient stain on it to cover the whole area of blood (about 8 or 10 drops are usually required). With a perfectly clean, dry, glass rod spread the stain over the whole film. About thirty seconds afterwards (and while the stain is still liquid) take the drop-bottle of distilled water in the right hand and a dry glass rod in the left hand, and add 10 to 15 drops of the distilled water, simultaneously mixing it with the stain by means of the glass rod. See that the stain and water are thoroughly mixed, and then allow the mixture to remain on the film for ten minutes or more. During this period use the glass rod again from time to time to ensure that the stain is distributed over the whole film and has not dried on any part of the slide. At the end of the time wash off the stain with distilled water and put the slide in a dish of distilled water for half a minute. Examine it under a low power to ascertain that the leucocytes are well stained and then dry it.

(5) Examine it under an oil-immersion objective, and note the following requirements of a well-stained film:—

(i) The red blood corpuscles should be a light transparent pink.

(ii) They should be quite free from "bubbles" and from deposited stain. Their outline should be clean and not smudged or broken.

(iii) The nuclei of the leucocytes should be an intense bright red. The protoplasm should be faintly blue and the red granules should show up clearly.

(iv) Blood platelets should be deep red.

Faults in making and staining films are often due to (*a*) leaving the drop of blood on the slide too long before spreading it; (*b*) not thoroughly drying the patient's finger, or the needle: (*c*) allowing the film to become partly hæmolysed by sweat from the patient's hand, or from one's own hand, or by inadvertently breathing on the slide; (*d*) incomplete fixation (the distilled water has been added to the stain too soon); (*e*) too old a stain, or impure methyl alcohol, or some fault in the distilled water; (*f*) the presence of grease on the operator's fingers.

(*c*) *Examination of the Film.*

Before commencing to study the appearance of malarial blood it is essential to be familiar with the appearances of *normal blood*, and the more common pathological changes. This axiom must be strongly impressed upon all who enter upon the microscopic study of malaria parasites. Many pages might be filled with an account of errors that have been made by observers who have mistaken for malaria parasites such normal constituents of the blood as blood-platelets, and even leucocytes —to say nothing of such common pathological changes in the red corpuscles as vacuoles, crenations, fissures, basophylia, &c.

(1) Examine a stained film from a case of malaria accompanied by severe anæmia. After focusing the red cells, find one of the straight edges of the film and pass under review all the structures along this edge. Search for and differentiate :—

Polymorphonuclear Leucocytes.—Note that the nucleus is large, irregular, and often apparently twisted; the body protoplasm faintly stained and with very fine granules.

Eosinophil Leucocytes.—With a bilobed nucleus (like two pears joined by their stems) and large eosin-coloured granules in the body protoplasm.

Small Lymphocytes.—Mononuclear; the round ruby red nucleus has only a thin rim of body protoplasm round it.

Large Lymphocytes.—The round nucleus is not much bigger than in the small variety, but there is a considerable amount of body protoplasm which often contains a few large dark red granules.

Intermediate Lymphocytes.—These are, in appearance, intermediate between the large lymphocyte and the *true large mononuclear cell.* The nucleus is slightly indented and there is a considerable amount of body protoplasm.

True Large Mononuclear Cells.—Large, usually oval, or blunt-pointed cells with clear, hyaline protoplasm and kidney-shaped nucleus.

Transitional Cells.—The nucleus is deeply indented or horse-shoe shaped; the protoplasm stains more deeply and is less hyaline than in the true large mononuclear cells.

Mast Cells.—With very large deeply red-stained granules throughout the cell and hiding the nucleus.

Myelocytes.—With round nucleus and many neutrophyl granules.

Blood Platelets.—Deeply stained ruby-red, scattered singly among, and on, the corpuscles, or collected in groups looking something like bunches of grapes. In malarial blood they are usually numerous and assume curious shapes and appearances. Beginners often mistake them for malaria parasites, especially when one of them is lying on a red cell, or when a group is arranged like "spores."

Red Corpuscles of different sizes and with different staining reactions.—Some cells may be swollen to double the size of neighbouring cells, others may be shrunken. Some may be stained blue instead of pink and may be stippled with very fine red and blue dots (Polychromasia); others may retain their proper colour but be stippled with fine blue spots (Basophylia).

Nucleated Red Blood Corpuscles.—Polychromatic red cells with a very deeply staining nucleus.

Red Corpuscles containing Benign Tertian Parasites.—The corpuscles are greatly swollen and are thickly stippled with bright pink dots (Schüffner's dots). Note that this stippling may be absent if the staining is faulty.

Red Corpuscles containing Malignant Tertian Parasites.—The corpuscles are of the same size or smaller than those near them and *may be* stippled with a few large irregular brick-red blotches (Stephens and Christophers' dots, sometimes called Maurer's dots).

Red Corpuscles containing Quartan Parasites.—The corpuscles are not altered in size[1] nor in colour, and are not stippled.

Artefacts and appearances simulating parasites.—These are many and can only be learnt by practical work. They are caused often by deposited stain, or by partial hæmolysis of the blood, or by faulty technique in making the film, or by contamination of the film with dirt or organisms from the patient's skin.

(2) At the risk of labouring the point, it must be repeated once again that learning to recognize in stained films the normal constituents of the blood and the various pathological changes just mentioned, should be the first task that the beginner will set himself seriously to undertake. Until that has been done the

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[1] According to Thomson and Woodcock corpuscles containing quartan parasites are often slightly smaller than normal corpuscles.

detection of malaria parasites, and of the other blood changes useful for diagnosis by microscopic examination cannot be approached with confidence; for it must be remembered that, although it may be easy, in class work, to find parasites in well taken and properly stained films, which are known to contain them, the problem is quite different when one receives for opinion a badly made smear or smudge of blood, from a patient on whom most of the drugs reputed to be good for "fever" have been tried.

(3) Having gained a good knowledge of the above subject, examine a well-stained film with a view to find and study the parasites. And here it may be mentioned that beginners make mistakes in regard to the finding of parasites not only because they are not familiar with the appearances of normal blood, but because they do not search in suitable cases at the commencement of their study. Some beginners expect to find parasites in every case of malaria—including chronic cases that have been drenched with quinine. Even a single dose of quinine (though it might not entirely stop the fever) will often cause all the parasites to disappear from the peripheral blood; and in blood films from patients who have received several doses an experienced observer very probably would not be able to find parasites, though he might find other evidence indicating the presence of the disease. This is why emphasis is laid on the desirability of never giving quinine to a patient suffering from fever until a blood film has been taken.

Therefore, when beginning the study of the appearances of the parasite in blood films, always choose a suitable case, namely, one in which quinine has not been tried and in which there are definite paroxysms of "ague" every other day or every two days.

As regards the actual search for parasites in a film it should be remembered above all that:—

(1) The parasite must be looked for *inside* a red blood corpuscle[1]—so-called, "free" parasites are almost never seen.

(2) The parasite has a very definite structure and appearance; if once seen it cannot well be mistaken for anything else; nothing that is at all "indefinite" is likely to be a malaria parasite.

In a film properly stained by the method described here, malaria parasites inside the red blood corpuscles are easy to detect.

Young "ring" forms of the parasite present the following characters:—

(1) A brilliant red dot at one part of the periphery.

(2) Adjoining or surrounding the red dot a clear unstained oval or circular vacuole-like area.

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[1] The beginner should hold this opinion firmly: later, when studying the marginal *accolés* or *appliqués* forms of the malignant tertian parasite he may permit himself to modify it.

(3) Surrounding the clear area a circle of blue stained protoplasm.

The red dot is the nucleolar chromatin and the circle of blue-stained protoplasm is the body of the parasite.

When one of these ring forms is found, measure its size with reference to the diameter of the corpuscle in which it lies. Is it less than quarter the diameter of the corpuscle? Note also whether the body of the parasite (the circle of blue) is thick or thin, whether it has thrown out any pseudopodial processes, and whether any fine grains of malarial pigment can be seen in it. Note also all the characters of the red cell containing the parasite, especially as regards its size, staining reaction, and the presence or absence of stippling (Schüffner's dots, Stephens and Christophers' dots, &c.).

Next find a large parasite about half or three-fourths the diameter of the red cell in which it is. Note that the three chief features are still present, namely: (1) a mass of chromatin; (2) a small "vacuolic" area adjoining it; (3) a large blue-stained body. Measure and draw the parasite and examine in detail the chromatin, the vacuole-like area and the blue body. Note that the chromatin is in a single mass, that the body has an irregular contour, or has thrown out definite pseudopodia, and that in the interior of the body tiny rods or dots of brown or black pigment (melanin) can be plainly seen. Describe the characters of the red cell as above.

Next find a form which nearly fills the corpuscle. The contour of the parasite is now round; probably the vacuole-like area cannot be made out; the chromatin, instead of being a single mass is in four or five large masses scattered through the body of the parasite; the pigment is much greater in quantity. This is the pre-segmenting stage of the parasite ("pre-sporulating" forms).

Next find a "sporulating" parasite. Perhaps the corpuscle may now be only a thin rim round the parasite, or perhaps the parasite may have "sporulated" before it quite filled the corpuscle. If "sporulation" is *complete* it will be seen that the chromatin, instead of being in four or five large masses, has now divided into perhaps from eight to twenty-three small round parts, each of which is surrounded by a separate mass of blue-stained protoplasm in which there is a small "vacuolic" area. It will be noted that each of the little bodies in the group has the same three characters as were characteristic of the parasite in its "ring" form, and that in the centre of the aggregation of young parasites there is a large block of malarial pigment which has been thrown out by the parasite in the act of division.

Intermediate stages between any of the above forms will be readily found.

All the forms described above belong to the *asexual* stages of the parasite—the stages which complete their life-cycle in the blood of man and cause the paroxysms of "ague" from which an infected person suffers. But the peripheral blood also harbours the *sexual* forms of the parasite which can complete their life-cycle only after being taken into the body of another host, namely, the *anopheline* mosquito

As these sexual forms alone are concerned in the spread of the disease from the infected to the healthy, through the agency of the mosquito, it is necessary to know how to recognize them in blood films. In comparison with asexual forms they are resistant, and may be present in the peripheral blood for some days after systematic quinine treatment has been commenced. As they do not cause fever or other obvious symptoms in man, their presence can be detected by blood examination only.

The characters of these sexual forms, when mature, are as follows :—

(1) *Round Forms, Male.*—A lightly stained parasite nearly filling the corpuscle. The corpuscle may be deformed and sometimes shows blunt processes, but the contour of the parasite within it is circular and without evidence of amœboid activity. In the centre of the parasite there is a large rather diffuse mass of lightly stained chromatin which shows no sign of division. This is surrounded by a clear unstained area, and outside this there is the circular lightly blue-stained body of the parasite in which little rods of malarial pigment are scattered evenly in a more or less concentric manner.

(2) *Round Forms, Female.*—These are larger than the male forms and stain more deeply. They have only a thin rim of the corpuscle round them. The chromatin mass is small, triangular in shape and always placed excentrically, usually touching the periphery of the parasite. Adjoining it is a clear unstained area. The body of the parasite is large and deeply stained, with coarse rods of pigment which may be more clustered together than in the male form.

These round forms are found in the benign tertian and quartan types of malaria only.

(3) *Crescent Forms.*—Large parasites, shaped like a bent sausage or a crescent moon, the ends of the crescent appearing to be joined together by the rim of the red blood corpuscle like the string of a bow.

Male Crescents.—The ends of the crescent are more pointed than in the female and the parasite stains a lighter blue. The malarial pigment is scattered in thick rods irregularly through the middle third of the parasite.

Female Crescents.—The ends of the crescent are rounded like a sausage. The parasite stains a deeper blue than the male. The chromatin is in a single mass in the centre of the parasite and the malarial pigment is aggregated in a compact circle round it.

These "crescent" or "sausage" forms are found in the malignant tertian type of malaria only.

(*d*) *Identification of Species.*

(1) Having learnt how to detect and describe the parasites in the red blood corpuscles, endeavour to ascertain the particular species of parasite that is present in the film under examination. The names of the three species usually recognized

as being definitely distinct have already been mentioned, and the particulars given in the following statement will enable them to be identified.

	Benign tertian. *P. vivax.*	Quartan. *P. malariæ.*	Malignant tertian. *P. falciparum.*
Stages found in finger blood	All stages	All stages	Only young "ring" forms and crescents. No large asexual forms.
Effect on the blood corpuscles	Corpuscles containing parasites are much swollen and may be stippled with Schüffner's dots	The corpuscles are practically unaltered in size or appearance	The corpuscles are generally decolorized and of the same size or slightly shrunken: never swollen. Maurer's dots may be present.
Amœboid movements of the parasite	Very active so that the parasite is irregular in shape and with long pseudopodia	Very sluggish, so that the parasite is generally oval or rectangular	Very active but with great tendency to assume the ring form. The rings are often marginal and may show two nuclear granules.
Number and arrangement of "spores"	20-23, often "like a rosette" but often arranged irregularly	8-10. Arranged with great regularity "like a daisy"	9-10 up to 24. They occupy only about half the corpuscle. Present in splenic, very rarely in finger blood.
Character of pigment..	Fine brown granules or rods	Coarse, very dark brown grains	Very fine dust-like specks difficult to see in the growing forms.
Sexual forms	Round; larger than the red cell.	Round: the size of the red cell	Crescent-shaped.

(*e*) *Evidence of Malaria when Parasites cannot be found.*

It would occupy too much space to describe the methods of carrying out examinations for this purpose and the subject cannot be learnt in the absence of practical demonstrations and much personal microscopic work. The three most important methods are:—

(1) The search for pigmented leucocytes.

(2) The differential count of the leucocytes.

(3) The search for macrophagocytic and endothelioid cells.

In these methods the value of the evidence rests entirely on the dependence that can be placed on the correctness of the observations made by the worker concerned. If an experienced observer, in whose knowledge of the subject one has confidence, reports that he has found a "pigmented leucocyte," the evidence that the patient is suffering from malaria is as strong as if actual parasites had been found. Secondly, if such an observer reports that by a differential count of the leucocytes (of which 500 or more should be passed under review) he has found a significant change in the percentage of mononuclear cells, his report would be of material assistance in favour of a diagnosis of malaria provided that other diseases and conditions in which a similar change occurs had been excluded. Thirdly, the finding in a peripheral blood film of even one or two macrophagocytic cells of a type which is not present normally in the periphera blood would be better evidence than is usually given by a routine "differential leucocyte count." I shall return to this rather difficult subject in the chapter on diagnosis

HOW TO FIND AND STUDY THE PARASITE IN THE INSECT HOST.

Before attempting to search for oöcysts in the midgut and sporozoites in the salivary glands of anopheline mosquitoes which have been caught in malarious localities it is essential to practise the technique of dissection and examination upon insects which have been bred out in the laboratory and fed upon healthy persons. This is the only way in which the appearance of various normal structures and secretions which are sometimes mistaken for zygotes and sporozoites can be thoroughly learnt. Thereafter it is necessary to have an opportunity of observing and studying zygotes and sporozoites in fresh dissections as demonstrated by one who is familiar with the subject. In the Tropics such laboratory demonstrations can be easily arranged in connection with work upon the malaria parasites of birds (Proteosoma), the zygotes and sporozoites of which in *Culex fatigans* closely resemble those of the human parasites in anophelines.

The following are some details in connection with work of this kind:—

How to study the Zygotes and Sporozoites of Proteosoma.

Select a sparrow which has been found by blood examination to be heavily infected with Proteosoma. Tie a small cloth hood over its head so that it is in darkness: it will then rest quietly. Place it in a mosquito-proof box like that shown in fig. 14, and add some male and female specimens of *Culex fatigans* which have been bred in the laboratory and have not fed. Next morning catch each mosquito in a separate test-tube and then release the sparrow. The mosquitoes which have fed will easily be recognized because their stomachs will be distended with blood. Attach a small piece of sponge soaked in water to the plug of each test-tube which contains a fed mosquito and place these test-tubes in an incubator at 80° F. Inspect them and change the piece of sponge daily until the mosquitoes have digested all the blood. When this is so it will be seen that the abdomen is quite white. Then repeat the feeding and daily inspection. When seven or eight days have elapsed since the beginning of the experiment kill and dissect in the following manner the mosquitoes which have become completely free from blood:—

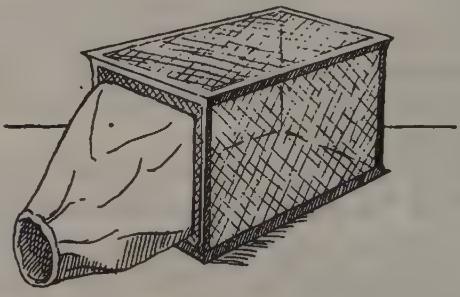

FIG. 14.

Allow a drop of chloroform to fall on the cotton-wool plug of the test-tube. As soon as the mosquito is dead turn it out into a watch-glass containing normal saline. After covering it with the solution pick it out, remove the wings and legs and place it on its side in a drop of saline on a glass slide.

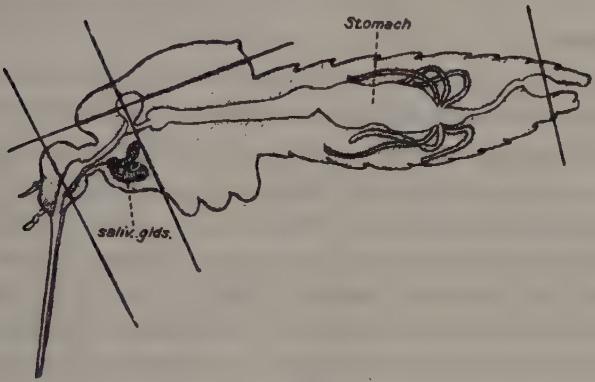

Fig. 15.

With a sharp knife (the knives used for cataract and other eye operations are best) divide the mosquito transversely across the thorax, as shown in fig. 15 above. With the point of a three-edged straight surgical needle pick up the head end of the mosquito (which contains the salivary glands) and replace it in the watch-glass of salt solution. Arrange the other portion of the mosquito ventral surface uppermost in the drop of salt solution on the slide, which should be laid on a piece of black paper. Using two needles nick the chitinous abdominal covering on each side at the junction of the terminal segments. Then lay one needle on the abdomen at this place and, with the other needle, fix the thoracic portion. Draw the two needles apart by intermittent dragging movements. The ovaries and the alimentary canal with its Malpighian tubes will remain attached to the last segment and will be plainly seen against the black background (fig. 16). Cut the alimentary canal across just behind the Malpighian tubes and discard the hinder end together with the ovaries. Using two sharp-edged needles cut away the Malpighian tubes one by one so that only the stomach of the mosquito remains. All this can be done without the aid of a dissecting microscope, but one may be used if found more convenient. Remove all pieces of tissue

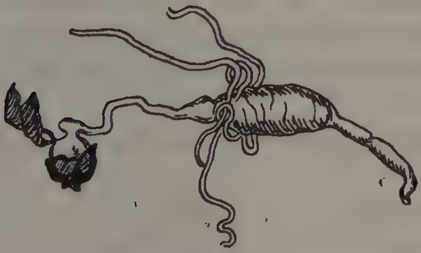

Fig. 16.

which might obscure the stomach, and apply a cover-glass. Tap the cover-glass gently so as to flatten out the stomach and then examine it first with a ¼ or ⅔-in. objective, and then with a ⅙-in. Zygotes, when of large size, will be readily seen. Their structure and the arrangement of the pigment in them can be studied with the $\frac{1}{12}$-in. oil immersion objective. Very young oöcysts can also be sought with this objective.

To make Permanent Preparations of a Stomach which contains Zygotes.

This is a delicate task on which the expenditure of much care and patience is well repaid. One must try as far as possible to keep the specimen quite flat and to prevent shrinkage of the stomach wall; and one must on no account allow the stomach to dry at any stage of the procedure adopted. I have obtained satisfactory preparations by the following method: With a ¼ or ⅙-in. objective find a zygote which is situated near the centre of the stomach. Place a large drop of cedar oil on the cover-glass and focus the oil immersion lens on the zygote. The pressure on the cover-glass will then be sufficient to keep the stomach flat throughout the subsequent procedure, which consists in passing the following solutions under the cover-glass with the aid of absorbent paper and fine pipettes. During these operations the pressure on the cover-glass can be regulated by using the fine adjustment, and the effect of the solutions on the zygotes can be watched.

(1) The fixing solution consists of:—

Saturated solution of corrosive sublimate	℥ i.
Absolute alcohol	℥ ii.
Glacial acetic acid	♏ iii.

Allow some drops of this solution to fall on the slide near one end so as to form a little pool which just touches the edge of the cover-glass, but does not flow over it. Using a fine pipette at the opposite edge of the cover-glass, draw this solution under the cover-glass so as to replace the salt solution. By this method continue to pass a stream of the fixing solution through the preparation for twenty minutes.

(2) Replace the fixing solution by 50 per cent. alcohol for fifteen minutes and by 75 per cent. alcohol for fifteen minutes.

(3) Replace with a solution of the following stain which has been kept some weeks:—

Saturated solution of hæmatin in 70 per cent. alcohol	10 c.c.
Alum solution (potash alum 50 grammes, water 1,000 c.c.)	250 c.c.

(4) Watch the effect of this stain on the zygote and other cells, and when slightly overstained replace with 50 per cent. alcohol for twenty minutes.

(5) Dehydrate completely with several changes of absolute alcohol.

(6) Clear with a stream of xylol. If there is any cloudiness dehydration has not been complete.

(7) Replace with xylol-balsam, which is the mounting medium.

To isolate the Salivary Glands for the Detection of Sporozoites.

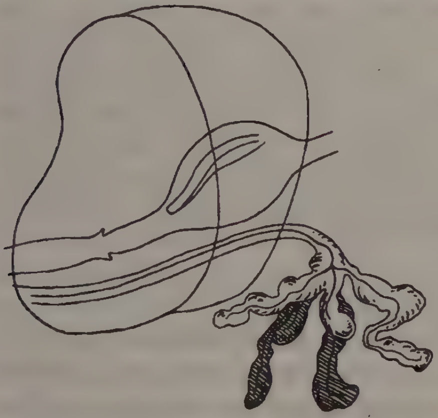

Fig. 17.

Transfer the head and anterior thoracic portion of the mosquito to a drop of salt solution on a slide under a dissecting microscope. Cut away the upper portion of the thorax longitudinally along the line shown in fig. 15. The glands lie in the lower front angle near the origin of the coxæ of the first pair of legs. Fix this part with one needle and insert the other needle in the neck of the mosquito just behind the head. Gently drag this needle away from the needle which fixes the thoracic portion. Transfer the slide to a microscope with a ¼-in. objective and see if the glands are attached to the head portion. They are glistening tri-lobed bodies easily recognized (fig. 17). Transfer back to the dissecting microscope and separate them at their junction with the head. If they are not attached to the head discard this portion of the preparation and examine the thoracic portion at the origin of the coxæ. Part of one of the lobes will probably be seen projecting from the mass of tissue, and, under the dissecting microscope, by pressure and slight teasing with the needles, the whole of at least one of the glands can usually be isolated. Before beginning to ascertain if sporozoites are present clear away all extraneous tissue so that the isolated gland will be the only object on the slide. Most mistakes are made because observers fail to exercise care and patience in this matter. When the gland is the only tissue present sporozoites are not difficult to observe. To find them apply a cover-glass over the gland and after getting it into the centre of the field of a ¼-in. objective turn on the ⅙-in. objective, allowing only a moderate light to pass through the specimen. When

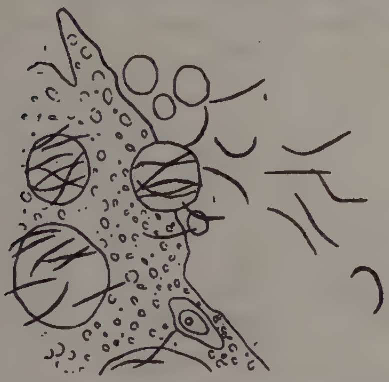

Fig. 18. (After Christophers).

it is in focus tap the cover-glass gently with the point of a needle. This will burst some of the gland cells and, if sporozoites are present, they will be seen pouring out of the gland cells as little sickle-shaped bodies among the droplets of gland secretions (fig. 18).

To make Permanent Preparations of Sporozoites.

When sporozoites have been found as above described insert the point of a needle under the edge of the cover-glass and tilt up the cover-glass so that it can be lifted off with forceps. Do not slide the cover-glass, but just lift it off. The gland may be on the cover-glass or it may have remained on the slide. Lay the cover-glass upside down on another slide. Allow the slide and the cover-glass to dry in the air. When completely dry stain both with Leishman's stain in the same manner as if they were blood-films. Mount them in neutral balsam. They can then be examined with the $\frac{1}{12}$-in. oil immersion lens and sporozoites will easily be found on both the cover-glass preparation and the slide.

HOW TO STUDY THE ZYGOTES AND SPOROZOITES OF THE HUMAN PARASITE.

When one has become familiar with this work on the Proteosoma parasite the appearance of the zygotes and sporozoites of the human parasite can be studied in anopheline mosquitoes which have been caught in malarious houses or have been designedly fed upon patients who have gametocytes in their blood. The method of carrying out a feeding experiment of this kind will be described in the next chapter under the heading "How to keep Mosquitoes alive." The method of dissection and examination is as above described.

CHAPTER IV.

The Practical Work necessary for Field Inquiry into Malaria (*continued*).

THE STUDY OF MOSQUITOES.

Mosquitoes (CULICIDÆ) are a family of small two-winged flies belonging to the order of insects termed DIPTERA. Systematic entomologists are not yet in agreement as to the best method of grouping the various members of the family, and it is fortunate that for the study of mosquitoes in relation to malaria it is not necessary to deal with that controversial subject. For our present purposes we can begin by stating that true mosquitoes possess the following characters:—

(*a*) They have a long proboscis which is adapted for sucking up fluids. In the female sex of most, but not all, species the proboscis is also adapted for piercing the skin.

(*b*) The arrangement of their wing-veins is characteristic.

(*c*) The veins on their wings are clothed with true scales.

These characters are illustrated in several figures on the following pages.

Although in all true mosquitoes the proboscis is long (usually about the length of the abdomen) and is adapted for sucking up fluids, by no means all species are blood-suckers, and no male mosquitoes have this habit. Many species feed on plant juices, and the members of one small genus have the very curious habit of living in association with ants which supply them with food.

The life of a mosquito is passed in four stages, namely: (1) the egg; (2) the larva; (3) the pupa; (4) the adult insect or *imago*.

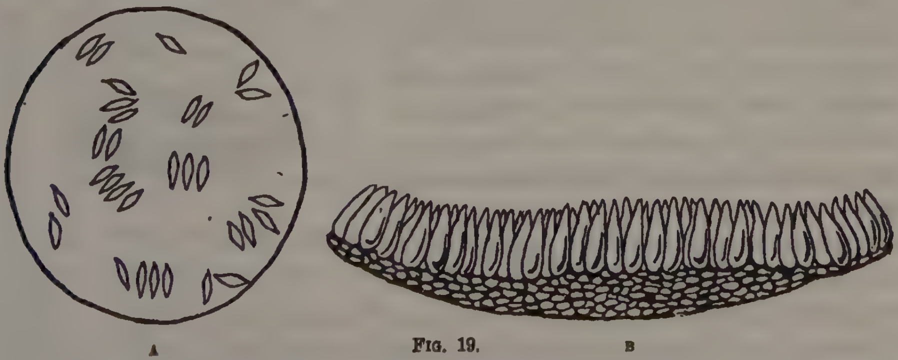

FIG. 19.

The eggs are laid by the adult female insect on the surface of water or on damp mud near water. They may be laid separately as in fig. 19, A, or in the form of a raft consisting of several hundred eggs joined together as in fig. 19, B.

The eggs float on the water for two or three days and then hatch into small wriggling animals called *larvæ.* These are very active free-swimming worm-like creatures which eat greedily and grow rapidly, casting their skins several times until they attain their full development. They can be found during the summer in almost every rain-formed pool and garden rain-tub. Unofficially they are named "wrigglers." Although their whole life is spent in water, they obtain the oxygen which they need, not from the water, but from the air. They obtain it by wriggling to the surface and projecting through the surface film a "syphon tube" which is situated at the tail-end of their bodies. When they rise to the surface to breathe in this way they look as if they were hanging from the surface film by means of this syphon-tube. The appearance is well shown in the above photograph (fig. 20) taken by Dr. Nash of some larvæ and pupæ of *Culex pipiens* (the common English house-gnat) which he found in a street gully at Wimbledon.

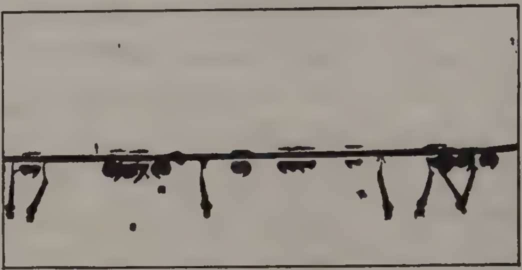

FIG. 20.—Larvæ and pupæ of *Culex pipiens.*

The time taken by the larvæ to complete their growth varies (with season and temperature) from a few days to several weeks. When fully grown they cast their skin again and become *pupæ.* In this stage their shape is like a comma with a very large head and sharply curved tail to the end of which two "paddles" are attached. Several are shown in the above photograph (fig. 20). During the pupal stage the insect does not eat, but the pupæ are active creatures which spend their life struggling to the bottom of the water and then floating gracefully to the surface again. Like the larvæ they breathe air through protruding spiracles, but these air-tubes, instead of being at the tail-end, are placed on the dorsum of the thorax as two trumpet-shaped structures projecting like horns. (See fig. 46, p. 66.)

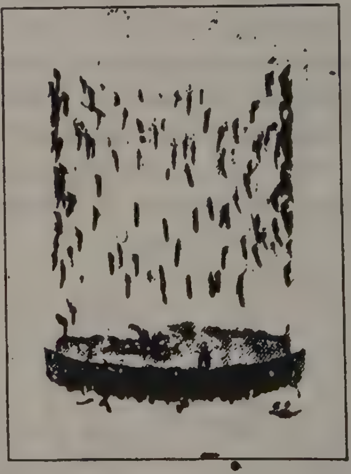

FIG. 21.

During the pupal stage profound anatomical changes take place within the pupal skin whereby the masticatory mouth parts of the larva are converted into the suctorial apparatus of the adult insect or *imago.* When these changes are complete the pupa comes to rest at the surface of the water; the pupa-case splits longitudinally down the median dorsal line, and the adult insect emerges, furnished with wings and legs adapted for life in the air. This is well shown in the accompanying photograph (fig. 21), also taken by Dr. Nash.

At present the family of mosquitoes contains about 1,000 species. All of them can be classed in one or other of the following groups:—

(1) *Proboscis* bent back in the form of a hook ... ... *Megarhininæ.*

(2) *Proboscis* straight
  - i. *Palpi* roughly as long as the proboscis in both sexes ... ... *Anophelinæ.*
  - ii. *Palpi* very short in both sexes ... *Ædinæ.*
  - iii. *Palpi* short in the female, long in the male ... ... *Culicinæ.*

In our present study we are concerned with mosquitoes belonging to the group ANOPHELINÆ, which alone contains species which convey malaria. In this group there are altogether about a hundred species, but up to the present hardly a third of them have been definitely found to be spreading malaria under natural conditions. Published lists of so-called "proved malaria-carrying species" should not be relied upon unless the evidence upon which the different species are named as being malaria carriers is clearly indicated.

The above general account should be sufficient to enable us to take up the practical study of mosquitoes first in the laboratory and then in the field. For this study we need in the first place: (1) A few dried specimens of mosquitoes; (2) a microscope and glass slides and cover-glasses; (3) entomological forceps and scissors; (4) a good hand-lens.

We may begin by describing:—

How to ascertain whether any particular Fly is a Mosquito or not.

Obtain a dried specimen of a mosquito of any species of either sex. With the point of a needle detach one of the wings at its origin in the thorax and allow it to fall on a microscope glass slide. Put over it a cover-glass, which should be kept in position by gumming strips of thin paper round its edge. Examine the specimen under the lowest power of the microscope, and see the long veins that pass from the base to the apex of the wing. Note that each of these veins is clothed with a double row of beautiful *scales*, and that the curved lower edge of the wing has a similar row (the "wing fringe") (fig. 22). Examine in detail under a higher power one or two of these scales that may have become detached in preparing the specimen. It will be seen that the scale is much longer than it is broad, that it is broader in the middle than at either end, that its apex is sharply pointed, and that a number of *striæ* pass as distinct supporting rods from the base of the scale to the apex. Using botanical terms to describe the shape of the scale, we should say it is oblong-elliptical.

Except certain of the *Psychodinæ*, or owl midges, whose general appearance is such that no one would be likely to call them mosquitoes, the mosquitoes are the only two-winged flies of which the wing veins and lower margin of the wing are fringed with scales in this manner.

Therefore when a fly is sent for identification the first thing to do is to examine a wing. If the wing veins and lower wing margin are clothed with scales the fly is almost certainly a mosquito. If the wing veins are bare, or are clothed with hairs instead of true scales, the fly cannot be a mosquito. (A hair, of course, tapers evenly from the base to the apex and has no supporting rods or striæ.)

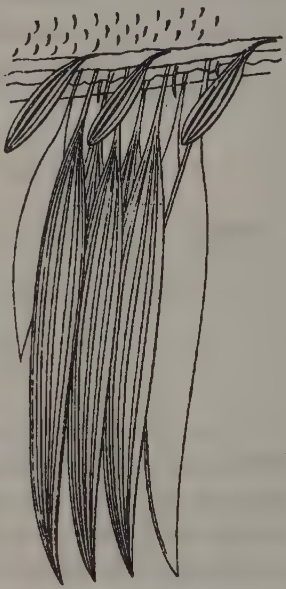

FIG. 22. (After Nuttall and Shipley.) The wing fringe.

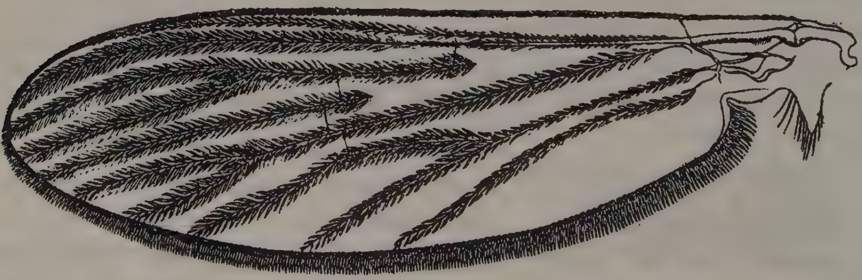

FIG. 23. (After Nuttall and Shipley.) Wing of *A. maculipennis*.[1]

The Arrangement of the Veins on the Wings.—With this specimen of a mounted wing we should next learn the arrangement of the wing veins which is characteristic of all mosquitoes. To do so, place the slide under the lowest power of the microscope so that, if possible, the whole wing will be in the field at the same time. At a first glance it will be seen that at the outer (apical) third of the wing there are two bifurcated veins separated from one another by a simple unbranched vein. Next follow out each vein from its origin at the base of the wing to its termination at the apex, comparing it with the drawing above and on fig. 28 (p. 42), which also gives the name of each vein.

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[1] Professor Nuttall has kindly permitted me to reproduce figs. 22, 23 and 27 from the *Journal of Hygiene*, vol. i, 1901.

The external or anterior border of the wing is the costa.

The first longitudinal vein runs parallel to the costa from the base to the apex of the wing.

The sub-costal vein (which is difficult to see) joins the first long vein to the costa.

The second long vein begins some distance beyond the base of the wing. After completing about half its length it divides into two branches—anterior and posterior.

The third long vein arises about the middle of the wing and is simple.

The fourth long vein begins at the base of the wing and divides in the last quarter of its length into anterior and posterior branches.

The fifth long vein also begins at the base of the wing and divides into two branches.

The sixth long vein arises at the base of the wing, is unbranched, and terminates about the middle of the posterior border of the wing.

The longitudinal veins are joined to one another by transverse veins which are shown on the left wing in the descriptive diagram (fig. 28).

The arrangement of all these veins must be learnt so that they can be drawn accurately from memory. After they have been drawn the position of dark areas on any of them (caused by dark-coloured scales) should be accurately inserted. They are of importance in identifying the particular species.

To study other structures of the mosquito it is necessary to mount the insect in the following manner:—

How to mount a Mosquito.

The following articles are necessary: (1) A supply of fine silver pins, No. 20 size; (2) a pair of forceps for holding the pins; (3) ordinary strong pins; (4) discs or squares of thin cardboard or celluloid; (5) a specimen box in the floor of which a layer of cork is fixed.

The method of mounting is as follows:—

(1) Take a disc or square and thrust one of the No. 20 silver pins through its centre so that about half the pin projects on each side.

(2) Through the edge of the disc, but in the reverse direction, thrust an ordinary pin which is to serve for fixing the specimen in the cork floor of the specimen box.

(3) Drop a little chloroform on the cotton-wool plug of the test tube containing the mosquito.

(4) When the mosquito is dead turn it out of the tube on to a sheet of cork or pith.

(5) With the point of a pin turn the mosquito on its back and insert the point of the No. 20 silver pin in the centre of origin of the legs. Use a hand lens to find this spot if necessary. Push the point of the pin through until it emerges in the centre of the dorsum of the mosquito's thorax. On turning the disc over, the mosquito will be found to be mounted with the dorsal surface uppermost, and the silver pin can now be withdrawn from the disc until the mosquito's legs touch the card. Then the legs and wings can be spread out with the point of a pin. The large pin should be thrust through a label before fixing it in the cork of the specimen box. (See fig. 24.)

This is the method of mounting mosquitoes which is usually adopted in museums, but there are some advantages in mounting them on rectangular blocks of pith (½ in. × ½ in. × ¼ in.) in the manner shown in the following drawing (fig. 25).

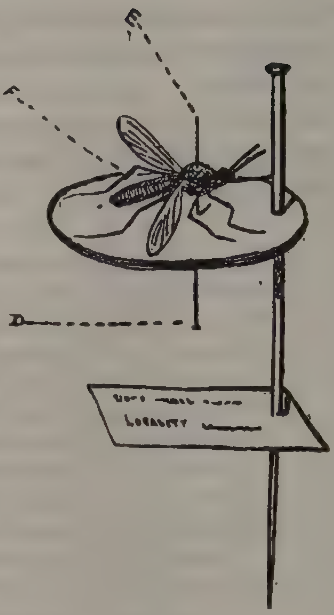


FIG. 24.

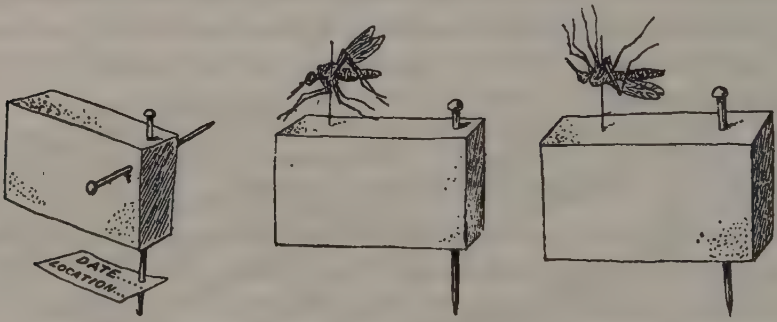


FIG. 25.

How to examine a Mosquito.

A low-power microscope is necessary for making a proper examination of mosquitoes.

(1) With sharp scissors cut off the head of the No. 20 silver pin obliquely so as to make a sharp point.

(2) From the underside of the card-disc push the silver pin upwards, and then on the upper side of the disc insert the forceps between the mosquito and the disc, and draw the silver pin (carrying the mosquito) completely out of the card. Fix the silver pin into the side or top of the cork of a specimen tube in such a direction that when the cork is laid on a slide under the microscope the dorsum of the mosquito can be examined (fig. 26). Change the direction in which the pin is inserted into the cork so that the particular structure that is being examined may be parallel to the stage of the microscope. Begin by examining one of the wings (to ascertain if the specimen is a mosquito), then the antennæ (to ascertain the sex), then the palpi (to ascertain the sub-family). Having noted the characters under these main headings, make a complete examination in the following order: Proboscis, palpi, antennæ, clypeus, vertex, occiput, nape (of head), dorsum of thorax, prothoracic lobes, scutellum, post-scutellum, abdomen, legs, wings.

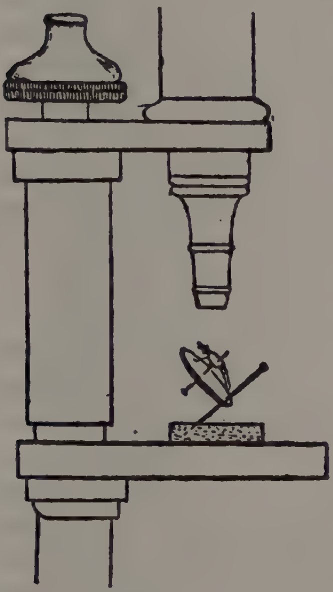


Fig. 26.

These structures are named in the following descriptive diagram (fig. 27), which Professor Nuttall has kindly permitted me to reproduce from the complete account of the structure and biology of *Anopheles maculipennis* which he and Professor Shipley published in the *Journal of Hygiene*, vol. i, 1901.

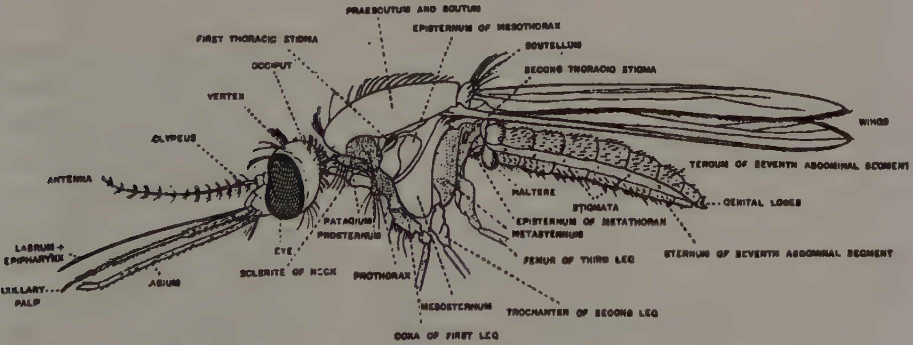


Fig. 27.—Side view of a female *Anopheles maculipennis*. (After Nuttall and Shipley.)

Most of the structures are also named in the descriptive diagram of a female anopheline mosquito (fig. 28, p. 42). On that diagram the clypeus is the median chitinous projection in the position marked "Frontal tuft." The prothoracic lobes or "patagia" are almond-shaped bodies situated one on each side of the anterior aspect of the prothorax. In order to find one of these bodies the mosquito must be turned partly on its side. Each prothoracic lobe carries hairs, and in some species a prominent tuft of scales projecting from the anterior border forms a useful character in identification. The scutellum is a prominent ridge running between the points of origin of the wings just behind the main dorsal area of the thorax. It carries hairs or scales. It may be only a simple ridge, or may show three definite projecting areas or "humps." In the latter case it is said to be trilobed. By focusing down from it the bare horse-shoe shaped post-scutellum or metanotum will come into view.

To put the different parts of the mosquito quickly under the microscope in such a position that they can be viewed satisfactorily, and their markings noted and drawn, requires a good deal of practice, but it is an essential preliminary to obtaining any useful knowledge about these insects. It is easier to put various parts under the microscope when the mosquito has been mounted on a block of pith than when card-discs are used. Thus from fig. 25 above it will be seen that in order to place a structure for examination parallel to the microscope stage it is not necessary to slant the pin at various angles; instead of doing so we can thrust a second large pin through the block at right angles to the first pin, and, when necessary, a third pin at an angle of 45° to the first pin. Again, for examining the ventral surface of the mosquito all we have to do is to grasp with forceps the silver pin which carries the mosquito, withdraw it from the pith and remount the mosquito upside down (fig. 25).

How to describe a Mosquito.

Begin by examining the proboscis, palpi and antennæ and work backwards, noting every marking and character which presents itself. As regards the palpi note the number, position and relative width of any white-scaled bands. Note whether, in addition to definite bands, any intermediate white-scaled patches are present on one or more segments of the palpi. For example, the description of the palpi of the mosquito (*Anopheles pulcherrimus*), figured on p. 43, would be: "*Palpi* loosely scaled with dark brown and white scales, and with four white bands. The terminal band includes the tip. Between the bands, the palpi are speckled with white scales." The *proboscis* would be described as being dark brown with a light tip, and the *antennæ* dark brown with silvery hairs and some white scales in the first six segments.

Next examine the head, noting the characters of the different groups of scales. We must look for: (*a*) Small narrow, curved, sharp-pointed scales (*n.c.* in the figures

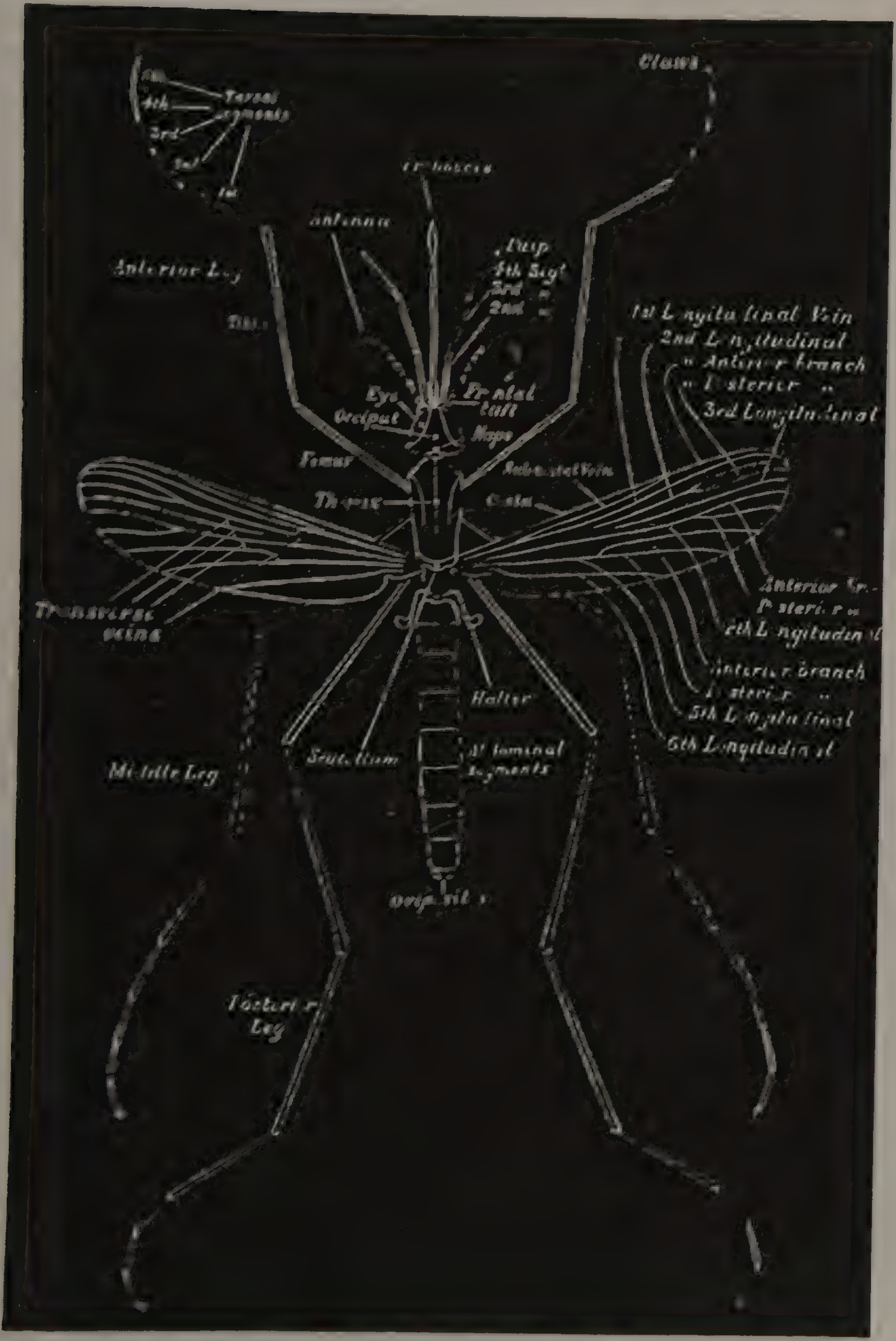


FIG. 28.—Descriptive diagram of a female anopheline mosquito.

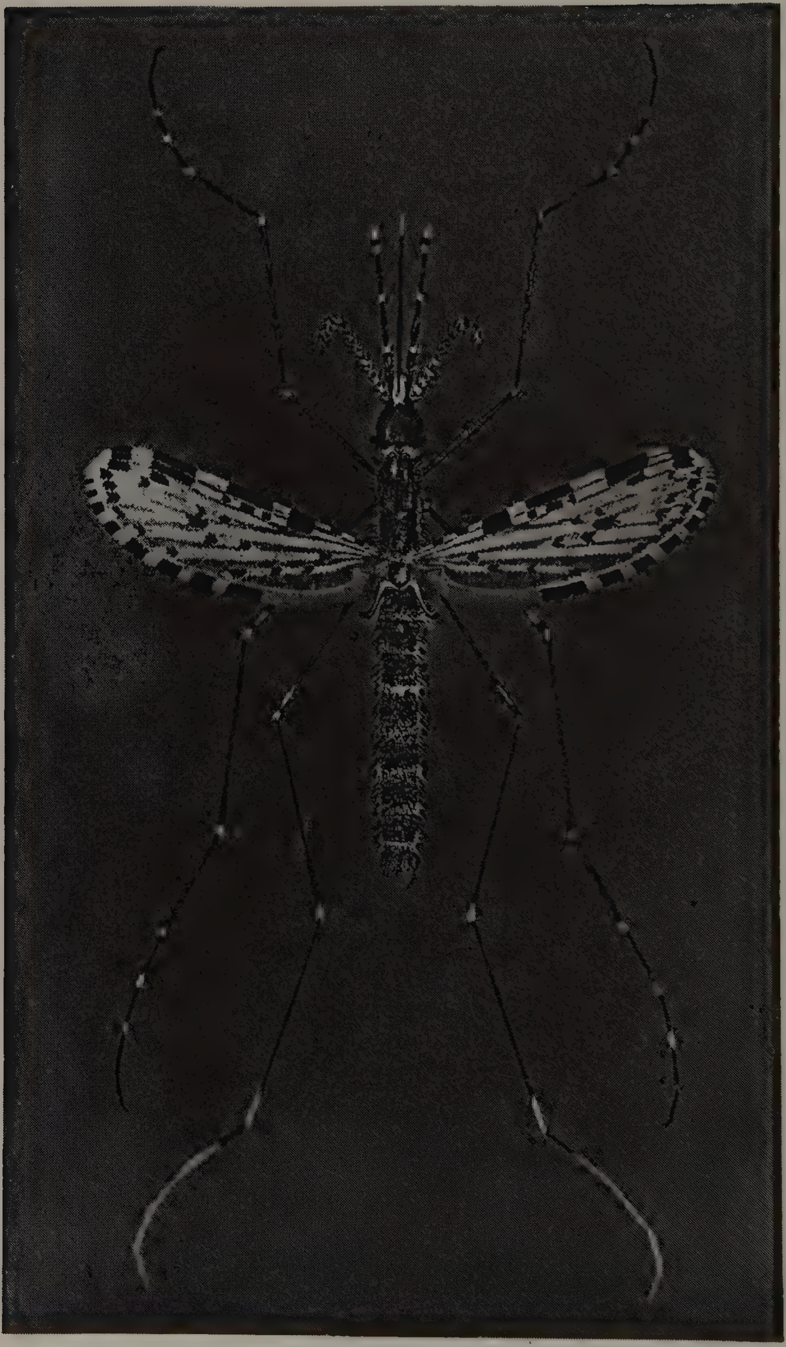
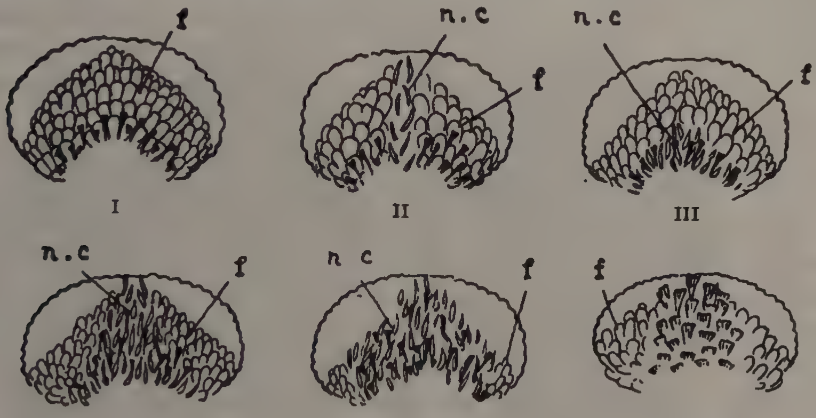


FIG. 29.—*Anopheles pulcherrimus* (female).

below); (*b*) flat, rather square scales closely appressed to the head and overlapping one another like the slates on a roof (*f* in the figures below); (*c*) upright expanding forked scales which are very obvious on the heads of nearly all mosquitoes. The following diagrams taken from an article by Major Christophers in *Paludism*, No. 3, July, 1911, show different groupings of these scales.



I II III

IV V VI

Fig. 30.

We should endeavour to ascertain in which of these groups the scale structure of the head falls. In No. I there are a few upright forked scales, but all the remaining scales are flat and closely laid on the back of the head like the slates on a roof. In No. II the head is covered with flat scales, but there is a median line of narrow curved scales. Some upright forked scales are also present. In No. III the head is covered with flat scales, but there is a small area at the nape with narrow curved scales. In No. V, which is the most common arrangement, the head is largely covered with narrow curved scales and upright forked scales, but there is a small area of flat scales low down on each side. Often this area of flat scales can be seen only by examining the lateral surface of the head. This is the arrangement in the common English mosquito *Culex pipiens* and the common tropical mosquito *Culex fatigans*. It is the arrangement also in many of the *Anophelinæ*, but in that sub-family upright forked scales greatly predominate over all other scales on the head. The following would be the description of the scales on the head of *Anopheles pulcherrimus* illustrated on p. 42: "Head clothed chiefly with broadly expanding upright forked scales which are brown at the sides of the head and pearly white on the nape, occiput, and vertex. Along the posterior border of the eyes superiorly is a row of flat overlapping scales and from the vertex a tuft of white linear scales and hairs projects forwards."

Next examine the thorax, noting the colour and character of the scales and hairs on the dorsum. The following drawing (fig. 31) shows on the left the dorsal surface of the thorax of *Anopheles rossii*, which is clothed with very narrow, curved, sharp-pointed tapering scales; and on the right the dorsal surface of the thorax of *Anopheles maculatus* which is clothed with quite broad creamy-white scales.

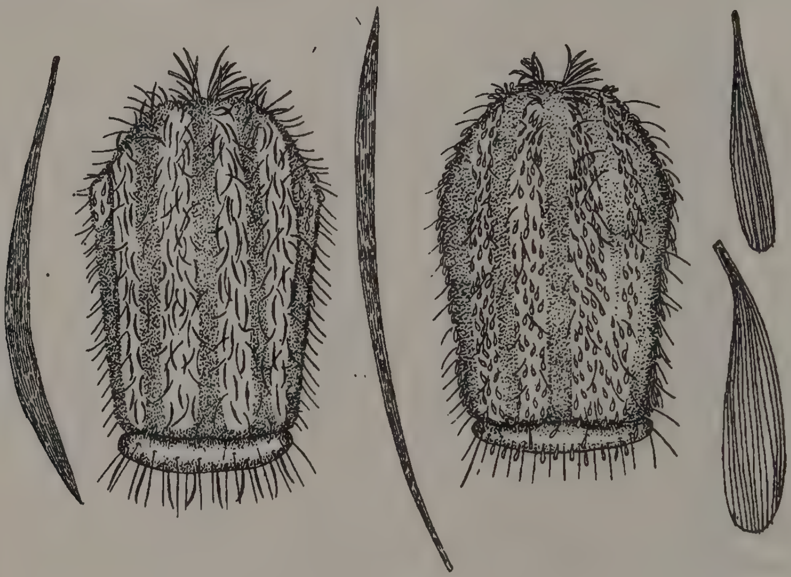


FIG. 31.

The *scutellum* is shown in the above figures as a simple bar or ridge just behind the thorax. This is its shape and appearance in all mosquitoes of the group *Anophelinæ.* It carries long bristles and sometimes a few scales like those on the thorax. In mosquitoes of other groups the hinder margin of the scutellum has three rather indefinite swellings or "lobes" and the scales which these lobes carry are of importance in identification. The following diagrams from the article by Major Christophers, mentioned above, illustrate the more common groupings.

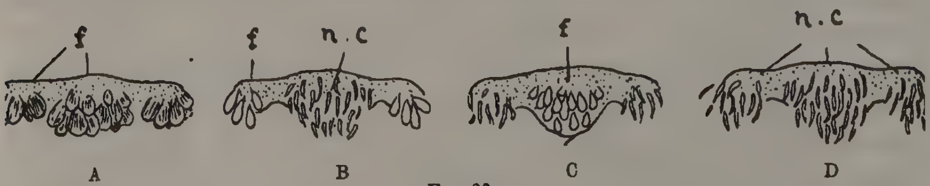


FIG. 32.

In A all three lobes have flat scales only; in B there are flat scales on the lateral lobes, narrow curved on the central; in C there are flat on the central and narrow curved on the lateral; in D all three lobes have narrow curved scales only. The last is the arrangement on the scutellum of the common English mosquito, *Culex pipiens.*

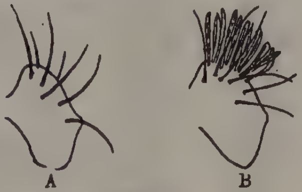


Fig. 33.

Complete the description of the thorax by examining the prothoracic lobes or patagia and noting whether they carry hairs only as in fig. 33 A, or whether they carry in addition a cockade or tuft of scales as in fig. 33 B. In representing them diagrammatically, they are usually shown as in fig. 34, which illustrates the dorsal surface of the thorax of *Anopheles kochii*, a species which is peculiar in having two dark eye-like spots on the anterior third of the dorsum.

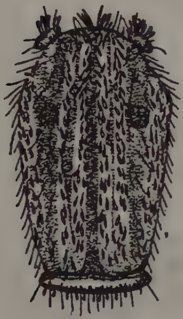


Fig. 34.

The description of the abdomen is of great importance. In the groups *Megarhininæ*, *Ædinæ* and *Culicinæ* each segment of the abdomen is clothed with flat, overlapping scales of various colours and sizes. In some members of the *Anophelinæ*, although the abdomen is thickly covered with long hairs no scales at all are present (*A. maculipennis*, *A. bifurcatus*, &c.). In others, in addition to the hairs which cover most of the segments a few golden-brown or dark-coloured scales will be found on the terminal segments. In others, every segment is thickly set with beautiful white or golden-brown scales which in some species are very broad, in others long and narrow. In others not only does every segment carry scales, but on some segments, either laterally or ventrally, additional scales are aggregated together to form prominent tufts, easily seen under a hand lens. The identification of species is greatly facilitated by an accurate description of this scale structure. The plate (fig. 35) on p. 47 illustrates various types of scale grouping found among Indian anophelines. Each drawing shows the abdomen from the dorsal aspect, from the ventral aspect and from the side, together with some of the individual abdominal scales as drawn with the aid of a camera lucida under a $\frac{1}{12}$-in. oil immersion objective and low eyepiece. The species illustrated are *Anopheles willmori* (Nos. 1 to 4), *Anopheles pulcherrimus* (Nos. 6 to 8), *Anopheles barbirostris* (upper right hand drawing), *Anopheles kochii* (lower right hand drawing). Diagrams of this kind convey a more accurate idea than written descriptions. The description of the abdomen of the species *pulcherrimus* (fig. 29) would be somewhat as follows: "*Abdomen* thickly clothed with very broad orbicular and rotundate[1] pearly-white

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[1] The nomenclature that botanists adopt for describing the shape of leaves. The terms have a definite significance and convey the same meaning to everyone who consults the figures of them given in any elementary book on botany.

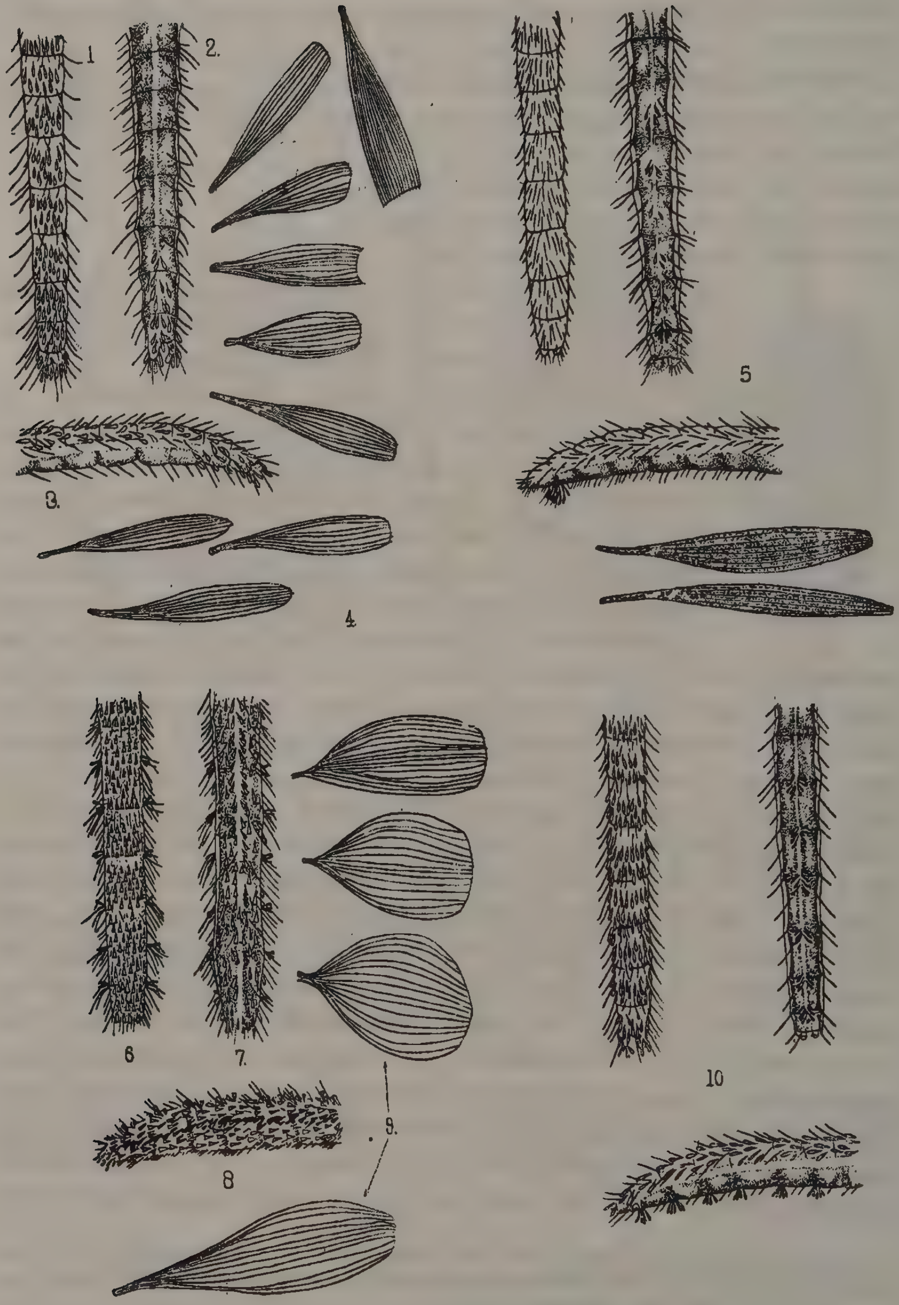


FIG. 35.

scales, which on the posterior borders of the segments project from the surface and overlap one another. In addition, from the postero-lateral corners of each segment a prominent tuft of dark brown scales projects transversely. The ventral surface is also clothed with broad white scales like those on the dorsum, but there are no ventral tufts."

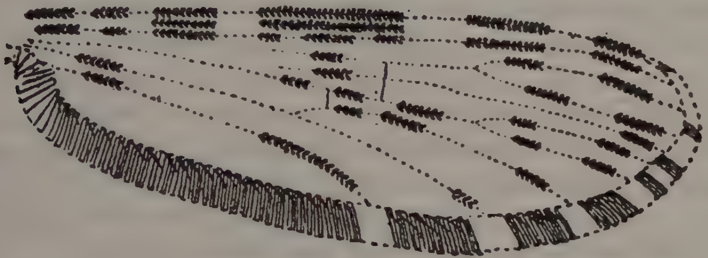


Fig. 36.—Wing of *Anopheles karwari*.

Next describe the wings. This is best done by means of a diagrammatic drawing giving the number and relative size and position of the different dark and light-scaled areas on each vein. The illustration of *pulcherrimus* on p. 43 is a descriptive diagram of this kind, and a drawing in simpler form is given here (fig. 36). To make such drawings it is often best to mount one wing under a cover-glass and examine it by reflected light.

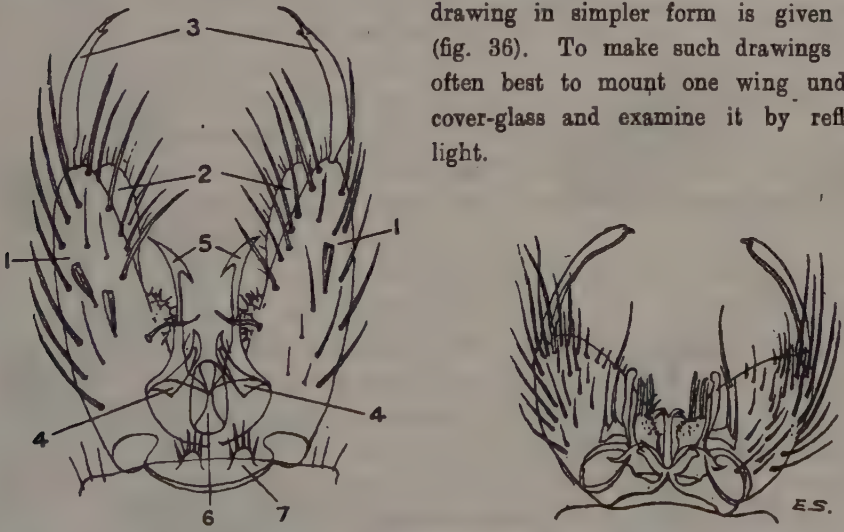


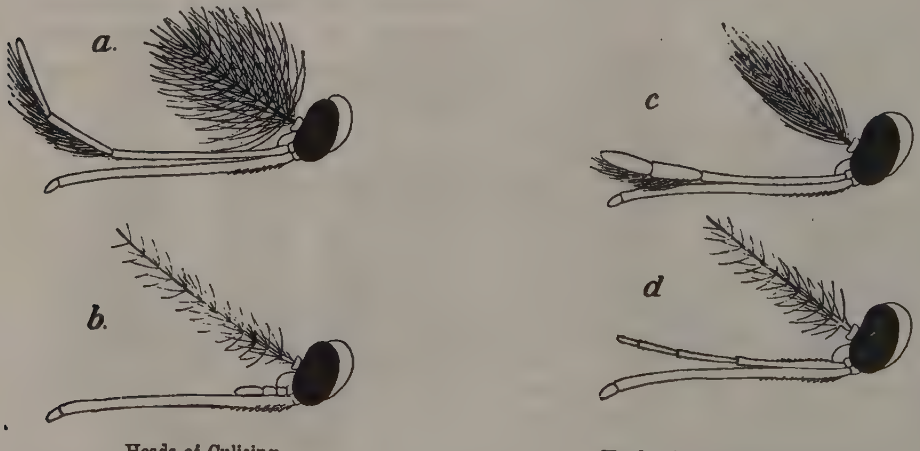
Fig. 37.—Male genitalia of a culex and an anopheles. (After Dyar and Knab.) 1, side-piece; 2, lobes of side-piece; 3, claspers; 4, harpes; 5, harpagines; 6, unci; 7, basal appendage.

Next describe each pair of legs in order, commencing with the markings on the femur and ending with those on the 5th tarsal segment. In many species complete bands of white scales encircle the legs near the joints. In addition small patches of white scales, not amounting to complete bands, may be found on some of the segments ("speckling"), and in some species one or more of the terminal tarsal segments of the hind legs will be found to be white-scaled in their whole length see the illustration of *pulcherrimus*, in which the last 3½ or 3¾ tarsal segments of the hind legs are white in their whole length).

The description will be completed by an examination of the male insect in the same way, with the addition, however, of a special description of the male genitalia, the characters of which are used by systematists for classifying and identifying mosquitoes. For this description it is best to snip off the terminal segment of the abdomen and mount it under a cover-glass. The drawing in fig. 37 gives the names of the different structures. The drawing on the left is of a male *Culex* mosquito; that on the right is of a male *Anopheles maculipennis*.

HOW TO IDENTIFY MOSQUITOES.

During the above examination and description the worker will become familiar with the different structures and the character of the markings by which mosquitoes are recognized and distinguished from one another. He can then proceed to the task of identification as follows:—



Heads of Culicinæ.
a, Male; *b*, female.

Heads of Anophelinæ.
c, Male; *d*, female.

FIG. 38. (Reproduced by permission from Sir Patrick Manson's "Tropical Diseases," published by Messrs. Cassell and Co., London.)

Assuming that the specimen has been proved by the above examination to be a mosquito, the next thing to do is to ascertain its sex. This is usually done by examining the antennæ. Male mosquitoes are "bearded," that is, the hairs at the joints of each segment of the antennæ are numerous and very long, so that each antenna looks like a little plume in front of the head. Female mosquitoes also have hairs at the joints of the antennæ, but these hairs are few and short, so that with the naked eye or under a low-power lens each antenna looks almost bare.

The sex can also be determined easily by examining the appendages on the terminal segment of the abdomen—the ovipositors in the female and the pair of long curved "claspers" in the male (3, fig. 37).

(2) Having ascertained the sex, the next point in identification is to determine whether the mosquito is a *Culicine* or an *Anopheline.* This is done by noting the length and characters of the palpi with reference to the length of the proboscis.

Assuming first that the specimen is a female, examine the palpi. If they are shorter than the proboscis the specimen is a *Culicine;* if they are as long as, or longer than the proboscis, the specimen is an *Anopheline.* (In female culicines the palpi are not more than about one-fourth or one-sixth the length of the proboscis or even less, but in a few species they may be half or perhaps nearly two-thirds the length.)

Assuming that the specimen is a male:—

(*a*) If the palpi are shorter than the proboscis the specimen is a *Culicine* of the group *Aedinæ.*

(*b*) If the palpi are as long or longer than the proboscis the specimen may be either a *Culicine* or an *Anopheline.*

(*c*) If the ends of the palpi are clubbed (fig. 39) the specimen is an *Anopheline*, if the ends of the palpi taper gradually to a point the specimen is a *Culicine.*

(*d*) Confirm by examining the scutellum. If the scutellum is only a single bar without indication of being made up of three parts or lobes, the specimen is an *Anopheline* (fig. 31, p. 45). If the scutellum has three projecting areas the specimen is a *Culicine* (fig. 32, p. 45).

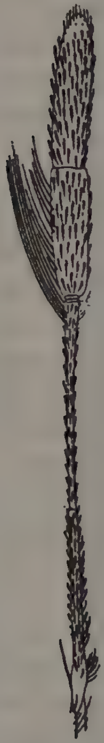


FIG. 39.—Palp of a male *Anopheles maculipennis.*

(3) Examine the abdomen of the common English culicine, *Culex pipiens*, and the abdomen of the common English anopheline, *Anopheles maculipennis.* Note that in *pipiens* (as in all culicines) each abdominal segment is clothed with a layer of flat scales arranged like the tiles on a roof, but that in *maculipennis* (as in some, but by no means all anophelines), the abdominal segments have no scales on them, but only long hairs.

(4) Having ascertained that the specimen is an anopheline, it is necessary next to determine its specific name. For this purpose we require complete and trustworthy descriptions with synoptic tables or "Keys to the determination" of all the

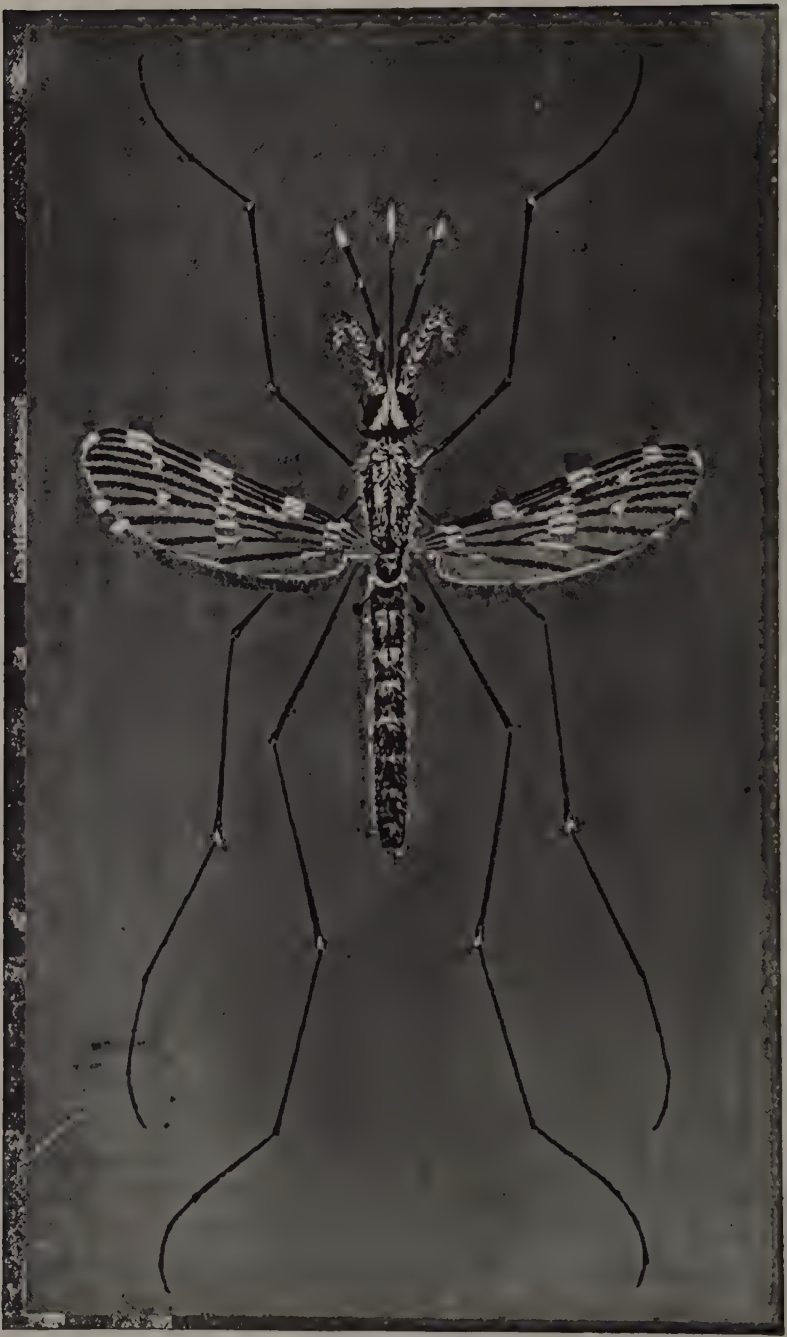


Fig. 40.—*Anopheles culicifacies* (female).

species and varieties which occur in the particular country concerned. With such descriptions and tables at hand all we have to do is to examine and write down the scale characters and colour-markings of the specimen to be identified and then hunt up in the "Key for determining species" the heading with which our description corresponds. Then compare the description, point by point, with the book description and diagrams.

It is of great assistance also to possess a set of typical examples of the anophelines of particular countries which have been identified and labelled by someone who is familiar with the subject and has had opportunities of seeing the "official types" of the different species which are sometimes deposited by their describers in the Natural History Department of the British Museum at South Kensington. Some years ago the Indian Central Malaria Bureau made it a practice to issue sets of typical examples to workers who desired them, and it would be very helpful if similar sets were available for other countries.

Failing such actual specimens the next best thing is to possess a set of drawings which record accurately in a diagrammatic manner the typical markings on the palpi, wings, legs and body of each species which occurs in the particular country concerned. The drawing of *A. pulcherrimus* on p. 43 and of *A. culicifacies* on p. 51 are examples of diagrams of this kind. They are reproduced from a noteworthy series of coloured drawings made by Dr. Turkhud of Bombay for reproduction in "A Monograph of the Anopheline Mosquitoes of India," by James and Liston (Thacker, Spink and Co., Calcutta).

With regard to further directions for actual identification it is not possible here to do more than give a few synoptic tables and indicate a few sources of information relating to the species in some countries.

ENGLAND.

In England only three species of anophelines occur, namely, *A. maculipennis*, *A. bifurcatus* and *A. plumbeus*. Their distribution, habits, &c., should be studied in the following publications:—

Journal of Hygiene, vol. i, 1901 (Studies by Professor Nuttall, Mr. Shipley and others).

"A Map showing the known distribution in England of the Anopheline Mosquitoes," by W. D. Lang. British Museum (Natural History), 1918.

"Reports to the Local Government Board on Public Health Subjects." New Series, No. 119, 1918, and No. 128, 1919 (contain reports and papers on malaria contracted in England during 1917 and 1918, respectively, and entomological information).

The following obvious characters serve to distinguish the three species:—

A. Wings with four dark spots	*A. maculipennis.*
B. Wings unspotted—	
1. Large, pale species; thorax brown with pale longitudinal markings...	*A. bifurcatus.*
2. Small dark species; thorax almost black with ashy-grey longitudinal markings	*A. plumbeus.*

Their Relation to Malaria.—Up to the present *A. maculipennis* is believed on epidemiological and experimental evidence to have been the responsible species in every case of locally contracted malaria which has occurred during 1917 to 1919 in England. The habits of the other two species in this country are not favourable to the spread of the disease, and although *bifurcatus* is a proved carrier in some other countries, it is certainly at present of very little danger in England.

FRANCE, GERMANY, ITALY, SPAIN.

The same three species are prevalent in the above countries, *A. maculipennis* probably being the chief agent concerned in the spread of locally contracted malaria. M. Roubaud has recently shown that specimens of this species collected in the environs of Paris are efficient hosts of both the Benign and Malignant Tertian parasites. In Southern Spain *Anopheles turkhudi*, which is a proved malaria-carrier, occurs.

THE EASTERN WAR AREAS IN EUROPE.

In Southern Europe, including Macedonia, the species reported are *maculipennis*, *bifurcatus*, *superpictus* (of which *palestinensis* is a synonym), and *pseudopictus*. Of these *superpictus* has been proved to be an active carrier, and during the war Wenyon found that both it and *maculipennis* carried the malignant tertian parasite.

ASIA.

Most of the Asiatic species of anophelines are included in the following synoptic table of species from India, Burmah and Ceylon, compiled by Major Christophers and published in the *Indian Journal of Medical Research*, vol. iii, January, 1916. This article brings up to date the information relating to various species which were described in "A Monograph of the Anopheline Mosquitoes of India," by James and Liston (Thacker, Spink and Co., Calcutta, 2nd Edition, 1911).

SYNOPTIC TABLE OF INDIAN SPECIES OF ANOPHELINI.

(*Arranged to include Variations of the Species.*)

1.	Wings unspotted ...	2.
	Wings spotted ...	5.
2.	Palpi banded ...	*A. immaculatus.*
	Palpi unbanded ...	3.
3.	Distinct white knee spots at apices of femur and tibia of hind legs; head scales broad ...	*A. plumbeus.*[*]
	No definite knee spots; head scales linear ...	4.
4.	Anterior forked cell nearly double posterior ...	*A. aitkenii.*
	Anterior forked scales relatively shorter ...	*A. culiciformis.*
5.	Costa with less than four dark spots involving both costa and first longitudinal ...	6.
	Costa with four dark spots involving both costa and first longitudinal ...	10.

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[*] The hill species *A. barianensis* (James) is regarded by Christophers as identical with the European species *A. plumbeus.*

6.	Inner half of costa without any pale interruption	7.
	Inner half of costa with pale interruption	*A. gigas.*
7.	Broad white band on femur	8.
	No broad white band on femur	9.
8.	White band on femur associated with scale tuft	*A. asiatica.*
	White band on femur without scale tuft	*A. lindesaii.*
9.	Palpi unbanded	*A. barbirostris.*[*]
	Palpi banded	*A. sinensis.*[†]
10.	Tip of hind legs not snow white	11.
	Tip of hind legs snow white	22.
11.	Femora and tibiæ not speckled	12.
	Femora and tibiæ speckled	19.
12.	Front tarsal joints not broadly banded	13.
	Front tarsal joints broadly banded	*A. rossii.*[‡]
13.	Tip of palpi black	*A. turkhudi.*
	Tip of palpi not black	14.
14.	Fringe spots not more than two	15.
	Fringe spots at all veins but sixth	16.
15.	No pale spots on veins other than those on costa	*A. rhodesiensis.*
	Pale spots at cross veins and bifurcations	*A. culicifacies.*
16.	Palps with two very broad white bands at apex	*A. minimus.*[**]
	Palps not so	17.
17.	Base of costa (inner quarter) entirely dark. Scales present only on front of thorax	*A. funestus* var. *listoni.*[††]
	Base of costa with one or more interruptions. Scales over at least half of thorax	18.
18.	Hind tarsi narrowly but distinctly banded (dark mosquito)	*A. jeyporiensis.*
	Hind tarsi not distinctly banded (light mosquito)	*A. nursei.*
19.	Not more than three spots on sixth vein	20.
	More than three spots on sixth vein	21.
20.	Palpi with one broad apical band	*A. ludlowii.*
	Palpi with two broad apical bands	*A. stephensii.*
21.	Hind legs with broad white band at tibio-tarsal joint	*A. leucosphyrus.*[‡‡]
	Hind legs not so	*A. tesselatus.*[‡‡]
22.	Hind legs terminated in an uninterrupted white area involving at least two whole tarsal segments	23.
	Hind legs not so. Only one tarsal segment or less wholly white	28.
23.	Abdomen with conspicuous lateral scale tufts	*A. pulcherrimus.*
	No lateral scale tufts	24.
24.	Femora and tibiæ not speckled	25.
	Femora and tibiæ speckled	26.
25.	Joint between first and second tarsal picked out with white. Scales on last two or three abdominal segments only. Border scales of wings fringe dark	*A. fuliginosus.*[‡‡‡]
	Joint not so picked out. Scales on most of the abdominal segments. Border scales light	*A. fowleri.*

[*] Beware of Malayan species, *A. umbrosus*, *A. albotæniatus*.

[†] Without fringe spot and small subcostal spot, var. *vanus*.

[‡] With apical white band on palp more than twice succeeding dark band, var. *vagus*.

[**] With pale proboscis and fringe spot at sixth, var. *aconitus*.

[††] Third vein mostly dark; wing as a whole very dark, var. *leptomeres*.

[‡‡] In these species the extreme tip of the last segment of the hind tarsus is white. As this may be overlooked they are placed in two positions in the table.

[‡‡‡] Two hind tarsi only completely white, var. *adiei*. More than one-quarter of the second hind tarsus white and fifth vein mostly pale, var. *nivipes*. Fifth vein pale, border scales pale, var. *pallida* of Theobald.

26.	Palpi with two broad apical bands	27.
	Palpi with one broad apical band	*A. jamesii.*
27.	Last three tarsal segments uninterruptedly white. Palpi speckled	*A. maculipalpis.*
	Only last two tarsal segments uninterruptedly white. Palpi not speckled	*A. theobaldi.*
28.	Last tarsal segment wholly white	29.
	Last tarsal segment not wholly white	31.
29.	Femora and tibiæ not speckled	*A. karwari.*
	Femora and tibiæ speckled	30.
30.	Scales (if present) on last few segments of abdomen only	*A. maculatus.*
	Abdomen covered with broad conspicuous scales	*A. willmori.*
31.	Half last tarsal segment white. Three spots on sixth vein	*A. kochi.*
	Extreme tip of last segment only white	32.
32.	Hind legs with broad white band at tibio-tarsal joint	*A. leucosphyrus.*
	No broad white band	*A. tesselatus.*

The Relation of the Indian Species to Malaria.—The most important carrier of malaria in nature in India is *A. culicifacies* (sporozoite rate 4 per cent. in Mian Mir, 8 per cent. in Ennur: Stephens and Christophers, 1901). The next most important carrier is *A. funestus*, variety *listoni*[1] (sporozoite rate 6 per cent.). Other proved carriers are: *A. fuliginosus* (the sporozoite rate determined by Adie was 1 in 200, by Fry 1 in 1,246), *A. ludlowi* (chiefly in the Andamans), *A. maculatus*, *A. maculipalpis*, *A. minimus*, *A. stephensi* (sporozoite rate in Bombay 3·5 to 10 per cent., Bentley), *A. willmori*.

The following notes relating to species in other parts of Asia may be added:—

In Palestine the common anophelines are *A. pharoensis*, *A. squamosus*, *A. turkhudi*, *A. superpictus* (of which *A. palestinensis* is a synonym), *A. mauritianus*, *A. maculipennis*, *A. bifurcatus* and *A. pseudopictus*. Of these species those not included in the above synoptic table of Indian anophelines will be found in the table of African anophelines which follows.

In Mesopotamia the species collected during the War were *A. pulcherrimus*, *A. stephensi*, *A. sinensis*, *A. palestinensis* and *A. maculipennis*. Christophers found that *A. stephensi* was the species chiefly responsible for spreading malaria in and near Basra.

In the Malay States there are about fifteen species, of which *A. minimus* (= *A. albirostris*, *A. christophersi*, *A. aconita*, &c.), *A. ludlowi*, *A. maculatus* and *A. umbrosus* are said to be the most important carriers.

In the Dutch East Indies the anophelines recorded are *A. ludlowi*, *A. rossi*, "*A. rossi indefinatus*," *A. aconitus*, *A. fuliginosus*, *A. jamesi*, *A. punctulatus*, *A. kochi*, *A. barbirostris*, *A. umbrosus*, *A. sinensis* and "*A. sinensis albipes*." Van Breemen has reported that in Batavia 1·3 per cent. of *A. ludlowi* caught indoors were found infected, and other observers have also found that this is the principal carrier in the country as regards both Benign and Malignant Tertian parasites.

In China *A. minimus* and *A. maculatus* are the chief carriers.

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[1] This species has usually been called *Anopheles listoni*.

AFRICA.

In the *Bulletin of Entomological Research*, vol. iii, November, 1912, Mr. F. W. Edwards gives the following:—

Key to the African Species of Anopheles.

1.	**Thorax with distinct broadish-elliptical scales (except in *A. christyi*); female palpi shaggily scaled; abdomen usually more or less scaly**	**2.**
	Thorax clothed with hairs or narrow almost hair-like scales; scales of female palpi usually appressed; abdomen without scales on the dorsal surface	**13.**
2.	**Abdominal scales obviously present on all the segments**	**3.**
	Abdominal scales absent, or if present, confined to the terminal segments ("*Nyssorhynchus*")	**8.**
3.	**Abdominal scales forming distinct projecting lateral tufts (*Nyssorhynchus*, [= *Cellia*])**	**4.**
	Abdominal scales not forming tufts (*Neocellia*)	**9.**
4.	**Last joint of hind tarsi light, or at least light-tipped**	**5.**
	Last joint of all tarsi entirely dark	**7.**
5.	**Last joint of fore and mid tarsi all dark; rather large yellowish species (5-6 mm.)***	**1. *pharoensis*.**
	Last joint of fore and mid tarsi light or light-tipped; smaller, less yellow species (4·5 mm. or less)	**6.**
6.	**Last joint of all tarsi wholly yellow; remaining joints regularly ringed with black and yellow; very small species (3 mm.)**	**2. *cinctus*.**
	Last joint of all tarsi white tipped; remaining joints not ringed; larger species	**3. *jacobi*.**
7.	**Hind tarsi entirely dark**	**4. *argenteolobatus*.**
	First four joints of hind tarsi with apical white rings	**5. *squamosus*.**
8.	**Last tarsal joint white; small species (3·5 mm.); Egyptian**	**6. *maculicosta*.**
	Last tarsal joint not white; large species (7 mm.); East African	**7. *christyi*.**
9.	**Hind tarsi entirely dark; three white palpal bands in ♀, the first two narrow**	**8. *brunnipes*.**
	Last two or three joints of hind tarsi white	**10.**
10.	**Four narrow white palpal bands; wing-scales lanceolate; legs spotted**	**9. *aureosquamiger*.**
	Three palpal bands, the last two rather broad; wing-scales much narrower	**11.**
11.	**Femora and tibiæ white-spotted**	**12.**
	Femora and tibiæ not white-spotted	**10. *rufipes*.**
12.	**Palpi white-spotted**	**11. *maculipalpis*.**
	Palpi not white-spotted	**12. *pretoriensis*.**
13.	**Abdomen with lateral tufts of very long slender scales on each segment (*Christya*)**	**13. *implexus*.**
	Abdomen without lateral scale-tufts	**14.**
14.	**Wing-scales mostly yellow, the black patches on the veins much reduced, but three long and one short black marks on the costa and first vein, the first two almost or quite united**	**15.**
	Wings not so marked	**16.**
15.	**Last 2¾ joints of hind tarsi white**	**14. *theileri*.**
	Last joints of hind tarsi dark	**15. *wellcomei*.**
16.	**Wings with at least three pale spots on the costal border (doubtful species are included in the next division) (*Myzomyia*)**	**17.**
	Wings with at most two pale spots on the costal border	**36.**
17.	**Last hind tarsal joints white; legs spotted**	**16. *natalensis*.**
	Last hind tarsal joints not white	**18.**
18.	**Femora and tibiæ more or less spotted with whitish; tarsi distinctly ringed at the joints**	**19.**
	Femora and tibiæ not at all white-spotted	**20.**

*** Unless otherwise stated, measurements denote the length of the body exclusive of the proboscis.**

19. Hind metatarsi with about five well-marked narrow whitish rings; female palpi with four narrow white rings ... ... 17. *ardensis.*
Hind metatarsi without distinct rings; female palpi with three white rings, the apical one broad ... ... 18. *costalis.*
20. Third vein with three dark and two light areas; male palpi with the club mainly yellow, as in *costalis* ... ... 19. *pallidopalpi.*
Third vein with only two dark areas (near base and apex), or entirely dark ... .. 21.
21. Palpi of female white only at the apex; base of first fork-cell nearer apex of wing than that of second; small, very dark species ... ... 20. *nili.*
Palpi of female with three or four white rings ... ... 22.
22. Third vein mainly (*funestus*, type form, and *culicifacies*) or entirely dark; mesonotum clothed with hairs ... ... 23.
Third vein mainly pale ... ... 26.
23. Hind tarsi with fairly distinct pale rings; wing-field with some pale spots ... 21. *longipalpis.*
Legs entirely dark ... ... 24.
24. Wing-field entirely dark; no pale scales even at bases of fork-cells ... ... 22. *rhodesiensis.*
Pale spots present at bases of fork-cells, even in the darkest specimens ... ... 25.
25. Lighter species, Mediterranean and Oriental ... ... 23. *culicifacies.*
Darker species (very variable), Ethiopian ... ... 24. *funestus.*
26. Palpi of female black-tipped ... ... 27.
Palpi of female white-tipped (in *A. cinereus* the white scales at the tip are easily rubbed off); mesonotum with narrow but fairly distinct scales ... ... 30.
27. No dark scales on first fork-cell or on anterior branch of second ... ... 25. *impunctus.*
Dark spots present (though sometimes small) on first fork-cell ... ... 28.
28. Vestiture of mesonotum consists of hairs ... ... 26. *hispaniola.*
Vestiture of mesonotum consists of narrow scales ... ... 29.
29. Third and fourth costal spots smaller; first fork-cell mainly pale-scaled ... 27. *chaudoyei.*
Third and fourth costal spots larger; first fork-cell mainly dark-scaled ... 28. *multicolor.*
30. Large joint of female palpi mainly dark, pale at each end; large species, wing-length about 5 mm. ... ... 29. *cinereus.*
Last joint of female palpi mainly or entirely white ... ... 31.
31. Tarsi dark; middle ring on female palpi rather narrow ... ... 32.
Tarsi with pale articulations ... ... 33.
32. Average wing-length 3·8 mm. ... ... 30. *transvaalensis.*
Average wing-length 3 mm. ... ... 24. *funestus.*
33. Larger (about 5 mm.); Mediterranean ... ... 31. *superpictus.*
Smaller; Ethiopian; middle and terminal pale rings on female palpi about equal and rather broad; tarsal joints with narrow yellowish rings ... ... 34.
34. Larger, darker species (3·5—4·5 mm.); third and fourth costal spots larger ... 32. *marshalli.*
Smaller, lighter species (3—3·2 mm.); third and fourth costal spots smaller ... ... 35.
35. A dark spot at apex of wing ... ... 33. *pitchfordi.*
No dark spot at apex of wing ... ... 34. *flavicosta.*
36. Thorax clothed with narrow scales; light spots on wings more numerous ... ... 37.
Thorax clothed with hairs (excluding the scales near the front margin); wings very dark, or else quite unicolorous ... ... 39.
37. The two last palpal bands (in female) about equal and rather broad—as in *A. marshalli*; tarsal joints with rather broad white apical rings ... ... 35. *austeni.*
Palpi of female with four narrow whitish rings; the terminal joint having a dark ring in the middle ... ... 38.
38. Numerous yellow forked scales on the head; legs dark, tarsi scarcely ringed ... 36. *distinctus.*
No yellow forked scales on head; femora and tibiæ spotted with whitish, tarsi distinctly ringed at the joints ... ... 18. *costalis* var. *melas.*
39. Last 2-3 joints of hind tarsi white; female with a tuft of scales on the ventral side of the last abdominal segment (*Myzorhynchus*) ... ...37. *mauritianus.*
Last joints of hind tarsi not white; female without ventral scale-tuft ... ... 40.

40.	Blackish species; wings with some pale spots	41.
	Lighter species; wings without any pale spots	42.
41.	Female palpi shaggily scaled; pale scales of wings occurring mainly on the fourth, fifth and sixth veins	38. *umbrosus.*
	Female palpi with appressed scales; pale scales of wings less numerous and occurring mainly on the first vein	39. *smithii.*
42.	Wings with dark spots formed by accumulation of scales	40. *maculipennis.*
	Wings without any dark spots	43.
43.	First fork-cell longer than second	41. *algeriensis.*
	Fork-cells of equal length	42. *antennatus.*

Their Relation to Malaria.—Of these species or varieties only a small number have been proved to be actively concerned in spreading malaria in nature. *Anopheles funestus* and its allies, especially *culicifacies*, are the chief transmitters, and probably *costalis* comes next in importance. In Egypt *turkhudi* and *superpictus* were probably the chief carriers during the War.

AMERICA.

The fourth volume of the "Monograph on the Mosquitoes of North and Central America," by Howard, Dyar and Knab (Washington, 1917), contains complete descriptions of nineteen anophelines from that country and the following key to their determination:—

TABLE OF THE SPECIES.

Adults, Structure, and Coloration.

1.	Tarsi ornamented with white or yellow	2.
	Tarsi wholly dark-coloured	13.
2.	Hind tarsi with a series of rings	5.
	Hind tarsi all white beyond second joint	3.
	Hind tarsi white beyond second joint, a black spot on the last joint	4.
3.	Abdomen dorsally covered with scales	*argyritarsis* Robineau-Desvoidy.
	Abdomen clothed dorsally with hairs only	*lutzii* Cruz.
4.	Palpi with the last two joints white except narrowly at bases	*tarsimaculata* Goeldi.
	Palpi with the last joint only white	*albimanus* Wiedemann.
5.	Hind tarsi with small basal rings only; palpi wholly black scaled	*grabhamii* Theobald.
	Tarsi more conspicuously ornamented; palpi not wholly black scaled	6.
6.	Tarsi and tibiæ narrowly ringed and speckled black and white or yellow	8.
	Hind tarsi with broad apical segmental white rings, not speckled	7.
7.	Wings with four white spots on the costa	*bellator* Dyar and Knab.
	Wings with two white spots on the costa, five on the first vein	*neivai* Howard, Dyar and Knab.
8.	Wing-scales mostly blackish, many little patches of yellow ones	*vestitipennis* Dyar and Knab.
	Wing-scales black and white or yellow, several large concrete patches of black scales	9.
9.	Hind tarsal joints with apical rings, the last joint wholly black	*maculipes* Theobald.
	Hind tarsi with rings involving both ends of the joints, last joint mostly or wholly pale scaled	10.
10.	Wing scales broad and rounded	11.
	Wing-scales narrowly ovate to lanceolate	12.
11.	Tarsi yellow with small black dots	*mediopunctatus* Theobald.
	Tarsi black with white rings	*malefactor* Dyar and Knab.
12.	Hind tarsi with numerous yellow rings	*strigimacula* Dyar and Knab.
	Hind tarsi with sparse white rings	*apicimacula* Dyar and Knab.

13. Hind tibiæ broadly white at apex ... ... *eiseni* Coquillett.
Hind tibiæ without white apical ring ... ... 14.
14. Wings with a white spot at outer third of costa ... ... 15.
Wings without such spot on the costa ... ... 16.
15. Palpi marked with white; third vein extensively white in the middle *pseudopunctipennis* Theobald.
Palpi wholly black scaled; third vein wholly black scaled ... ... *punctipennis* Say.
16. Wings with patches of yellowish scales, sixth vein with three black spots *crucians* Wiedemann.
Wings without patches of pale scales ... ... 17.
17. Wing at apex with a coppery spot on the fringe ... ... *occidentalis* Dyar and Knab.
Wing-fringe uniformly dark throughout ... ... 18.
18. Body blackish throughout, hair-scales of mesonotum dark brown ... *atropos* Dyar and Knab.
Body not wholly blackish, hair-scales of mesonotum yellow or white ... ... 19.
19. Palpi of the female with dull silvery white rings at the bases of the joints; scales of wings not distinctly massed at bases of fork-cells ... ... *walkeri* Theobald.
Palpi of female blackish scaled throughout; scales of wings massed to form distinct spots at the cross-veins and at bases of fork-cells ... ... *quadrimaculatus* Say.

Of these species *quadrimaculatus* and *occidentalis* are closely allied species very similar to, if not identical with, the European *maculipennis;* and *walkeri* and *barberi* are closely allied species very similar to, if not identical with, the European *plumbeus*.

Relation of the American Species to Malaria.—Messrs. Dyar and Knab note that the list of malaria transmitters given in the first volume of their Monograph was compiled from lists which are "far from reliable," and in view of the critical study of the literature which would be necessary they are not prepared to give a revised list. In the Panama Canal zone, according to Darling, *A. albimanus* was, in 1908, by far the most important agent in spreading the disease; while *A. pseudopunctipennis* was only slightly concerned in transmitting it, and *A. malefactor* not at all. The remaining eight species of anophelines which had been collected in the zone were rare and in all probability only exceptionally had opportunities of conveying malaria. In Northern Louisiana Bruce Mayne in 1917 found *A. quadrimaculatus* infected in nature to the extent of 2·4 per cent. He also found one specimen of *A. crucians* infected among twenty examined. In Florida Metz found zygotes in the stomach wall of two specimens of *crucians* caught in nature (379 examined).

Important Malaria-carrying Species in Different Countries.

In most countries one or two species are much more actively concerned with the spread of malaria than others. Major Christophers has compiled the following list of species which he considers (on account of their known habits, carrying powers, relative prevalence and widespread distribution) may be regarded as the chief malaria-carrying species in the countries named. It should, perhaps, be emphasized that the list by no means includes *all* the malaria-carrying species in the particular countries, but only those which have been most frequently found to be responsible for the spread of the disease.

In Europe and North America: *A. maculipennis* and its allied species *A. quadrimaculatus* and *A. occidentalis.*

In Southern Europe: *A. superpictus* and *A. bifurcatus.*

In the United States: *A. quadrimaculatus* and *A. crucians.*

In Central and South Tropical America and the West Indies: *A. albimanus* and *A. argyritarsis.*

In Southern Spain and North Africa: *A. turkhudi.*

In Greece, Asia Minor, Palestine, &c.: *A. superpictus.*

In the Mediterranean: *A. pseudopictus.*

In Mesopotamia: *A. stephensi.*

In India: *A. culicifacies, A. listoni, A. stephensi,* &c.

In the Malay States: *A. minimus, A. maculatus, A. ludlowi.*

In the Malay Archipelago and New Guinea: *A. leucosphyrus* and *A. tesselatus.*

In North Australia: *A. annulipes.*

Throughout Africa and in Southern Arabia: *A. funestus* and *A. costalis.*

In some forest regions: *A plumbeus* (Europe), *A. lutzii* (Central America).

STUDY IN THE FIELD.

How to Collect Adult Mosquitoes.

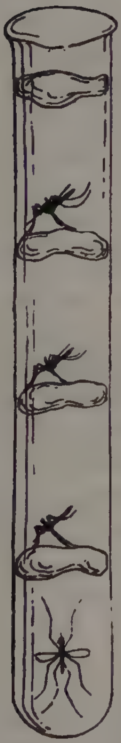

FIG. 41.

After a systematic study of the adult insects in the laboratory take up their study in the field. The following are methods for collecting them alive:—

(1) Carry in your pockets or haversack two dozen dry test-tubes, a supply of cotton-wool, a long pencil, and a small folding entomological hand-net, and proceed to search for adult mosquitoes that are resting on the walls, rafters and ceilings of cowsheds, stables, outhouses, tents, huts and dwelling rooms. Examine carefully cobwebs hanging from the rafters or in dark corners. When a mosquito is seen resting, place the mouth of a test-tube very gently over it. Keeping the mouth of the tube pressed against the wall move the tube sideways. This will dislodge the mosquito which will fly to the other end of the tube, and then the mouth of the tube can be

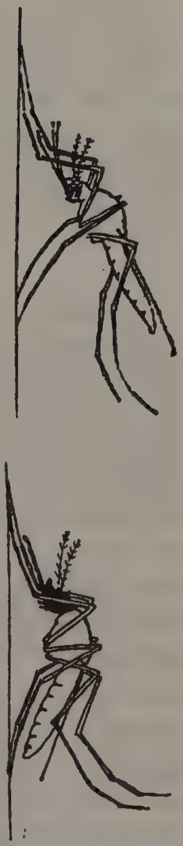

FIG. 42.

plugged with cotton-wool. With the long pencil push the plug down the tube until the imprisoned insect has only about an inch of space in which to fly about. Then use the tube to catch another, and plug in the same way. Continue in this manner until the tube holds four or five insects each in a separate compartment (fig. 41). If a mosquito takes flight while you are preparing to put the test-tube over it endeavour to catch it in the hand-net, or wait until it settles again.

(2) With a co-worker, sit near a pool or streamlet in a wood during the afternoon or early evening, and catch in test-tubes the mosquitoes that alight on his hands and clothes.

(3) For other methods of collecting adult mosquitoes, see pp. 70, 74 and 103.

During the collection of mosquitoes in houses anophelines can often be recognized by the fact that they rest with the proboscis, head, thorax and abdomen in a straight line, while culicines usually rest in a hunch-backed position. This point is illustrated in fig. 42, but it is best not to place much reliance upon it, but to catch all the mosquitoes which can be seen, and afterwards to examine them properly in the laboratory.

How to keep Mosquitoes alive and to feed them.

(1) Take a wide-mouthed bottle with a hollow ground-glass stopper. Fix the stopper upside down on a thick piece of wood which will serve as a stand when the bottle is placed upside down over the stopper. Dry the bottle thoroughly, and push into it a bent piece of white cardboard of such size that, when straightened out inside the bottle, it will be fixed in a sloping position. Half fill the stopper with water and float on the water a piece of cork covered with white paper. Transfer some mosquitoes from the test-tubes into the bottle by the following method: Tie a piece of thick paper over the mouth of the bottle. In this cover cut a half-circle valve of the same size as the mouth of a test-tube. Take the tube that contains the mosquito and put its cotton-wool plug over the paper valve. Draw away the cotton-wool, and at the same time insert the mouth of the tube through the valve into the bottle. When the mosquito has flown into the bottle, draw out the tube and at the same time plug the valve with the cotton-wool. When there are several mosquitoes in the bottle turn it upside down over the stopper (which has been prepared as described above) and carefully slide away the

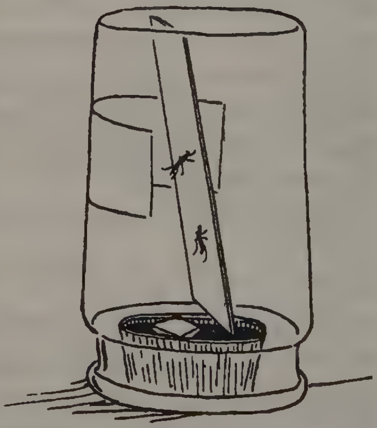

FIG. 43. (After Christophers.)

paper cover. In a bottle of this kind, kept in a dark cupboard, mosquitoes, if fed regularly, will live a long time and will lay their eggs on the water and white paper floating on it. Fig. 43 illustrates these so-called "mosquito hotels."

To feed the mosquitoes proceed as follows: Lift the bottle partly off the stopper and insert a piece of thick paper between the stopper and mouth of the bottle. Hold the paper so as to close the mouth of the bottle and turn the bottle over. Lay a piece of mosquito netting on the top of the paper. Lay the palm of your hand on it and draw away the paper, leaving the netting as a cover to the mouth of the bottle. Tie the netting on tightly. Take the bottle with you to bed, and place it under the bedclothes so that your forearm rests over the netting that covers the mouth of the bottle. By morning most of the mosquitoes will have gorged themselves with blood. They should be fed in this way every three or four nights. When the mosquitoes have fed replace the bottle over its prepared stopper and slide away the netting.

The eggs laid by a mosquito in one of these bottles should be removed to a dish of pond water. They will hatch into larvæ, which should be reared to the pupal and adult stages. In this way one can study and describe accurately the character of each stage in the life-history of any particular species.

Mounting and Despatch of Specimens.

The method of mounting mosquitoes described on p. 38 is used only when it is desired to preserve good museum specimens. Ordinarily in field work it is sufficient to impale the mosquito with a No. 20 silver pin of which the head has been removed by an oblique cut with a pair of sharp scissors, no card-disc being used. Mosquitoes thus mounted are usually arranged in rows on a piece of cork in tubes like that shown in the following figure (fig. 44).

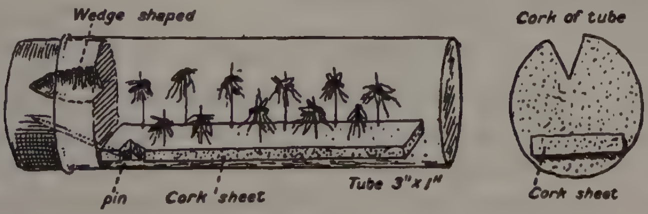

FIG. 44.

These tubes, each wrapped in cotton-wool and packed in a box can be sent through the post with safety. Useful practical details on this and other subjects connected with the study of mosquitoes will be found in Nos. 1 to 5 of the publication *Paludism*, which was issued by the Committee for the Study of Malaria in India.

STUDY OF LARVÆ AND PUPÆ: HOW TO COLLECT THEM.

Take a cup, a spoon and some corked specimen tubes or small bottles with wide mouths. Examine all collections of water likely to harbour mosquito larvæ. Use the following methods of search:—

(1) Kneel or squat by the side of the pool and carefully examine the surface of the water.

(2) With a stick, or your hand, stir up the mud from the bottom of the pool and endeavour to wash larvæ away from the roots and stems of vegetation in which they shelter. After doing this thoroughly for some minutes let the water come to rest and watch for larvæ as they rise to the surface. They are very easily seen in muddy water. Dip them out with the spoon.

(3) With an enamel saucer or cup dip under the weeds at the edge of the pool and in backwaters and eddies of streamlets.

(4) With a calico net stretched on an iron ring sweep under the weeds and plants growing in the centre of the pool. Every few minutes turn the net over into a flat dish of water and wash all the larvæ into the dish. (See also p. 76.)

(5) Using glass tubing about the size of a lead pencil, and having a piece of rubber tubing attached, suck up the water from holes in trees and from the axils of leaves.

Larvæ and pupæ dipped out with the spoon should be poured into a specimen tube or bottle.

In the laboratory transfer all pupæ to a jar half full of water, on which float a few leaves or bits of grass, and tie mosquito netting over the mouth of the jar. Place the jar near a window but not in direct sunlight.

Place the larvæ in a basin of the pond water exposed to direct sunlight and change the water every few days. Do not cover this basin, but examine it each day for pupæ and transfer them to the covered jar.

DESCRIPTION OF LARVÆ.

The larvæ of all mosquitoes are made up of: (1) The head, (2) the thorax, (3) the abdomen. The abdomen has nine segments, of which the first seven closely resemble one another. The eighth segment carries the external openings of the respiratory tubes or *tracheæ*, by means of which the larva obtains oxygen from the air.

The structural differences between the larvæ of anopheline mosquitoes and the larvæ of other kinds of mosquitoes will be seen at a glance on examining fig. 45 below.

In all anopheline mosquitoes the two large tracheæ open directly on the upper surface of the eighth segment by two stigmata which are surrounded and supported by a complex apparatus (A in fig. 45). In the larvæ of all other kinds of mosquitoes the respiratory tubes do not open directly at the surface of the segment but are prolonged onwards into a projection called the syphon tube (B, fig. 45). Again, on the dorso-lateral surface of some of the abdominal segments of anopheline larvæ a pair of characteristic structures called "palmate hairs" are present (C, fig. 45). Each of these hairs has a short stalk to the apex of which are jointed a number of leaflets which, when opened, form an apparatus somewhat like an umbrella which

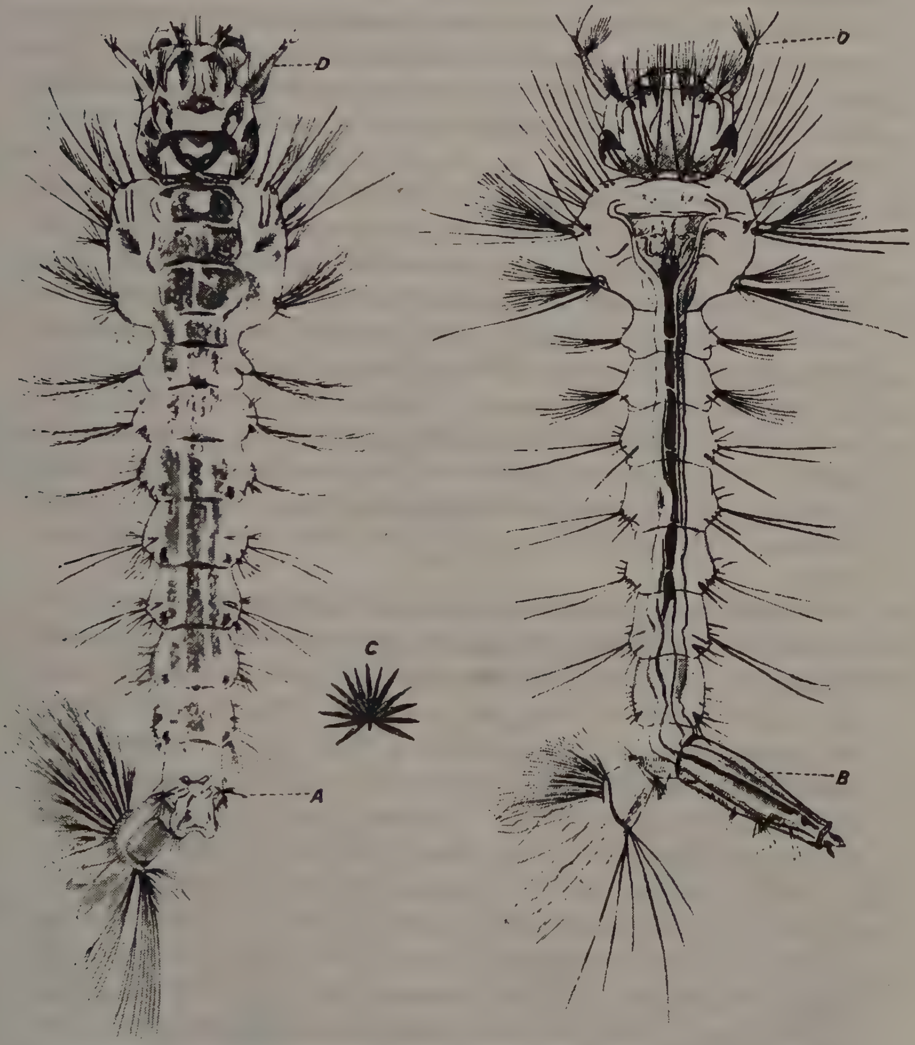

Fig. 45. (After Dyar and Knab.)—Larva of *Anopheles punctipennis*. Larva of *Culex quinquafasciats*.

has been turned inside out. When the larva comes to the surface these palmate hairs break the surface film, open out, and so keep the larva floating parallel to and just beneath the surface. They are not present on the larvæ of any other kind of mosquito than anophelines. By these characters the larvæ of anophelines can be easily recognized. Having no syphon tube, and being provided with palmate hairs, they float in the water immediately beneath and parallel with the surface film. The larvæ of other mosquitoes, because they have a syphon tube and are not provided with palmate hairs, float considerably below and at an angle of about 45° with the surface film.

The head of an anopheline larva is more or less conical in shape and is covered with a clearly defined chitinous case. The rudimentary eyes are placed laterally, and in front of each is an eminence which carries the antenna (D, fig. 45). The antennæ of anopheline larvæ are of simpler structure and carry fewer hairs than those of culicine larvæ. The anterior median area of the head of anopheline larvæ is called the clypeus and on each side of this there is a large bunch of hairs called the "whorl organs" or "feeding brushes." Lying directly over each whorl organ is a hair called the external frontal or external clypeal hair and between the whorl organs is a pair of hairs close together called the median frontal or clypeal hairs. These four frontal or clypeal hairs project beyond the head and may be simple or branched. Their characters are used in the identification of different species of larvæ.

The aquatic larvæ of other flies than mosquitoes may sometimes be mistaken for mosquito larvæ. There are, for example, the larvæ of the flies called *Chironomus*, *Ephemera* and *Dixa*. Chironomus larvæ are often found in large numbers when the mud at the bottom of a small pond is stirred up. They are bright red worm-like creatures which are commonly known as "blood worms." Although their tracheæ open externally in a pair of "respiratory tubes" their appearance is quite different from that of mosquito larvæ. The larvæ of the *Ephemeridæ*, or May flies, differ essentially from those of mosquitoes in that their air-tubes do not open externally, so that they obtain the oxygen from the water by means of gills, the presence of which makes them easily recognized. In the larvæ of the *Corethridæ*, also, there is no direct communication of the air tubes with the external air. The larvæ of this kind of fly are very transparent, and are called for that reason "phantom larvæ." The head is much smaller than that of any mosquito larva. The larvæ of the *Dixidæ* bear a superficial resemblance to anopheline larvæ and float just beneath the surface film as the latter do. But all the segments of Dixa larvæ are almost equal in size, and the larvæ possess four prolegs, by using which they creep up the side of the vessel in which they are placed. Moreover, they have no palmate hairs.

How to examine Larvæ.

With a rubber-teated pipette, or a spoon, transfer a culicine and an anopheline larva to a watch-glass and examine them with a hand-lens. Describe the differences that can be seen with the naked eye. Note that the anopheline larva at the surface always swims backwards and that it moves by jerks. Watch the action of the feeding brushes and see that in order to feed at the surface film the larva twists its head smartly through an angle of 180° so as to bring the ventral surface uppermost.

(2) With a pipette transfer an anopheline larva in a drop of water to a glass slide and gently imprison it under a cover glass. Put it under a low power of the microscope and watch the action of the feeding brushes again. When the larva has drawn in its feeding brushes endeavour to see four hairs that project from the clypeal or frontal area of the head. Two of them are central and easily seen; they may be slightly branched or frayed at the tips. The other two are situated one each side under the feeding brushes which, when protruded, hide them.

Examine the abdominal segments and (if the dorsal surface of the larva is uppermost) see the pair of "palmate hairs" on each segment. Count and draw the leaflets of one of these little fan-shaped structures. Note that these palmate hairs are not present in culicine larvæ.

Note the difference between the antennæ of a culicine and an anopheline larva.

THE PUPÆ.

The pupæ of anophelines and culicines are not easily distinguished from one another. In anopheline pupæ the two thoracic breathing trumpets are short, stumpy and funnel-shaped. In culicine pupæ they are often long and slender. (Fig. 46 below.)

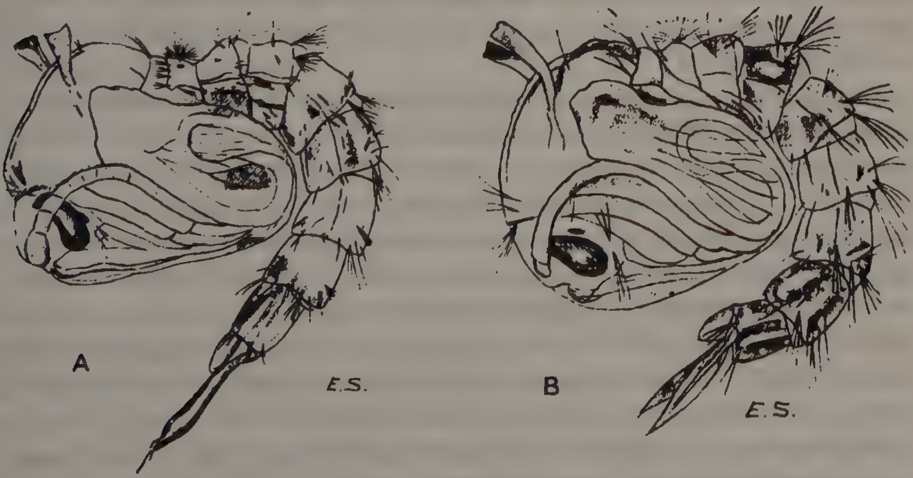

FIG. 46.—A, Pupa of *A. punctipennis*. B, Pupa of *C. pipiens*. (After Dyar and Knab.)

The Eggs.

How to examine Eggs.

When a female anopheline has laid some eggs on the white paper and water in the stopper of the prepared bottle before described, place the stopper on the stage of the microscope and examine the eggs under a low power. Note the tiny frill or rim that encircles the margin of the upper surface of the egg, and describe the lateral floats.

When a few of the eggs have hatched, mount in glycerine those that remain; some of them will show the larva emerging from the eggshell.

Fig. 47 A shows the upper surface of an egg of *A. maculipennis.* The inner edges of the floats are widely separated and they appear to arise from the tiny rim of air-cells which surrounds the edge of the egg. Fig. 47 B shows the same egg from the side. The upper surface of the egg is flattened, the lower is rounded like a boat and is marked with polygonal areas. The rim from which the floats arise is more clearly seen.

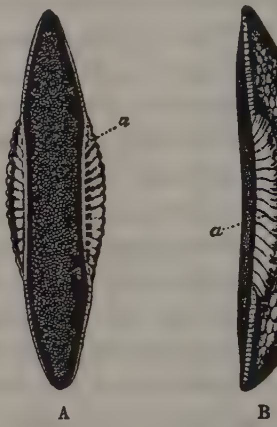

Fig. 47. (After Nuttall.)

THE HABITS OF MOSQUITOES.

In the attempt to provide a groundwork of information upon which the study of mosquitoes can be begun in a satisfactory manner this chapter has already extended beyond the limits which were contemplated. I can therefore refer only very briefly to the very important subject of the habits of mosquitoes and the methods by which they should be studied.

Unfortunately information upon the life-history and habits of mosquitoes is at present rather unsatisfactory because it is so often given in the form of broad generalizations which are assumed to apply to the whole family of mosquitoes, instead of as facts relating only to the particular species in regard to which the observations were made. The idea that in general all kinds of mosquitoes have the same life-history and habits is wrong, and there can be no doubt that the first step towards making real headway in measures for their reduction is a complete study of each species separately. Such a study may show that it is justifiable to group certain species having similar habits together, but it will also indicate very clearly that the habits of some groups are entirely different from those of others, and that quite different measures are necessary for dealing with the members of its various groups.

In the following notes I shall, whenever possible, name the particular species concerned.

Swarming and the Act of Pairing. The First Flight.—The remarks under this heading will refer to the common English anopheline *A. maculipennis.* When the adult insects of this species take flight after emerging from the pupal stage their first act in nature is governed by the sexual instinct. The males congregate in groups called "swarms," which on calm evenings can be observed in gardens, hay-fields and other suitable places about 8 to 20 feet above a flower bed or other object. The swarm performs a kind of mazy dance which in the mating habits of mosquitoes is thought to play a part similar to the "display" of males in the mating of birds. "Observers who have watched a swarm of male mosquitoes tell us that, sooner or later, into the midst of the swarm bounces a female. A regular scuffle ensues and in a few seconds the female, with the male she has secured, drops out of the swarm, which then gradually resumes its rhythmic motion, in anticipation of another irruption" (Mr. M. D. Lang).

The Second Flight.—The fertilized female *A. maculipennis*, after separating from the male, now seeks a place in which to pass, in well-being and safety, the period required for the maturation of its eggs. In all probability this instinct to find a place of permanent safety is more pronounced, and is manifested earlier, than the instinct to obtain food, for with this species (and most others which suck blood) the desire to bite is seldom manifested until the second day after birth. The instinct to find a "permanent home" results in the insects' "second flight" which may be of the nature of a definite "migration" to localities a mile or more from the place where the insects were born. The flight is continued until a place suitable for permanent stay is found. In the case of *A. maculipennis* such a place must be one in which the mosquito can readily obtain meals of blood, but except in so far as the sense of smell, or of heat, or of any other condition in the environment, governs the direction of flight, the sense of the need of food is perhaps not manifested until the insect has found a safe home.

Third and Subsequent Flights.—Assuming that a female *maculipennis* has settled down in a suitable place, her subsequent flights are no more than are necessary for obtaining regular meals of blood and of water, and when the eggs are mature, for the purpose of laying them. It is probable that after each of these short flights the insect returns to the place which she first selected as a "permanent home."

The "Homing" Instinct.—One of the most interesting observations which has been made on the epidemiology of malaria in England relates to the finding of "malarious houses," in which the occurrence of an indigenous case of malaria is followed at intervals during the same season by other fresh cases in that particular house and family. The explanation seems to be that a mosquito (*maculipennis*) which has lived long enough to become infected has also acquired the habit of remaining for some weeks or months in that house, *or of returning to it after every flight.*

Æstivation and Hibernation.—Mosquitoes are greatly affected by temperature. In the tropics the adults of all species die very rapidly if they are exposed to direct sunlight, and in very cold countries the adults of all species die when winter sets in. Between these two extremes the adaptability of the insects to heat and cold differs with each species, but in all species the females are more adaptable than the males. In some desert areas in the tropics no breeding takes place during the hottest months of the year when all pools are dry and all the male insects have died, but the females of some species, e.g., *funestus*, continue to live in a very sluggish condition hidden away in buildings, holes in trees, &c. ("æstivation"). In cold countries at the onset of winter all the males of most species, and all the females of some species, die off, but as regards other species the females continue to live, in a condition approaching that of "hibernation," by hiding in sheltered places. In England females of *A. maculipennis* can be found throughout the winter in cellars, church towers, stables, &c., but few, if any, females of *A. bifurcatus* survive the winter.

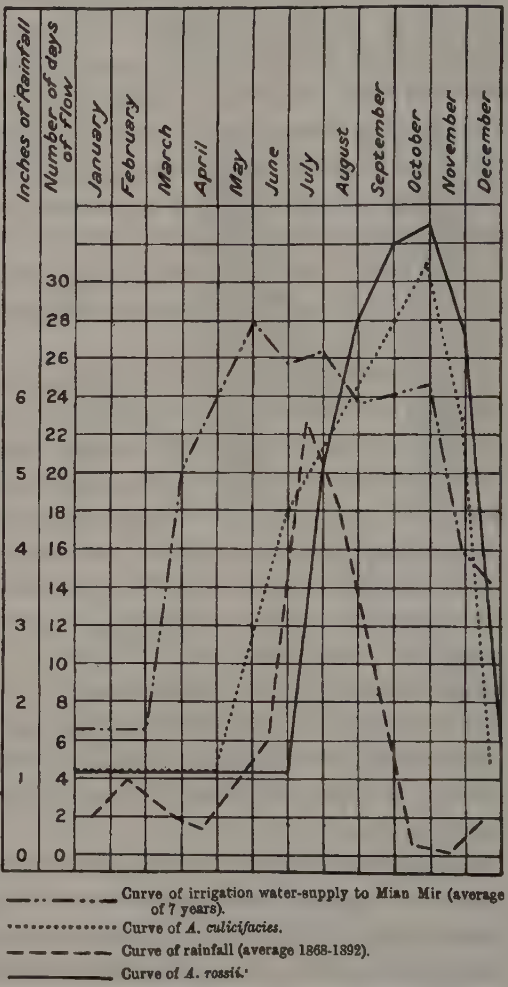

FIG. 48.—The incidence of anophelines correlated with irrigation and rainfall.

Species which cannot exist in the adult form at certain seasons of the year pass through those seasons in the larval stage (e.g., *A. bifurcatus*, *A. plumbeus* and *A. culicifacies*) or in the egg stage (e.g., *Stegomyia fasciata*).

Seasonal Prevalence.—For these and other reasons, connected chiefly with the environment, mosquitoes have, in most countries, a very definite seasonal prevalence which differs with different species. This must be worked out separately for each species and correlated with the various factors on which it depends, as is shown, for example, on the preceding chart (fig. 48).

Numerical Prevalence.—Observations upon mosquitoes are of very little value unless they take numbers into account. For this reason in an area in which these insects are being studied a certain number of "observation stations" should be selected and visited regularly with the object of counting the number of adult mosquitoes of different species which can be caught in them in a definite time. In this way Mr. A. J. Grove has worked out week by week the numerical prevalence of *A. maculipennis* in certain areas in England. His results should be read in the "Reports and Papers on Malaria contracted in England in 1918" (Local Government Board Public Health Reports, New Series, No. 123, 1919), but the following chart (fig. 49) roughly indicates the seasonal incidence of adult *A. maculipennis* in one of his observation areas.

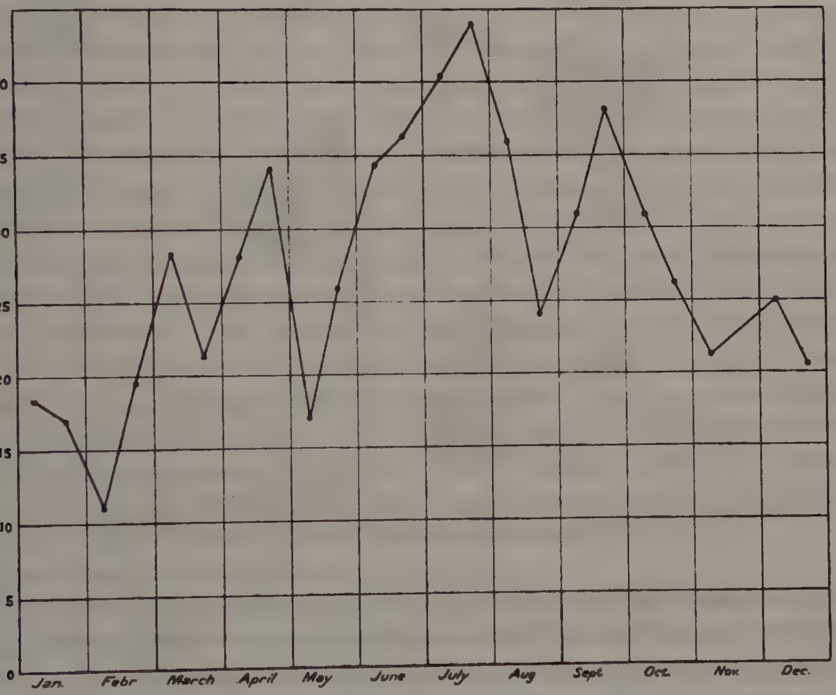

FIG. 49.—Seasonal incidence of adult *A. maculipennis* in New Romney, Kent.

Catching in test-tubes is not a very suitable method for species which live mostly out of doors. For such species it is useful to employ a trap of the kind shown in the following photographs (fig. 50).

These traps consist of a rectangular wood framework 5 feet long, 3 feet deep and 3 feet broad, closed with mosquito netting, one end of the trap being a door on hinges. The traps are placed on the ground in a shaded corner of a garden and are covered with sacking and a thick tarpaulin so that the interior may be dark and cool. Two or three pots of plants are placed inside each trap and several near the door which is left partly open. The traps are set overnight. In the morning about 8 or 9 o'clock the vegetation in the vicinity of the traps is disturbed as much as possible and straw and paper torches are burnt in all the surrounding outhouses and buildings so as to drive the mosquitoes into the open air. The result is that most of the insects quickly find their way into the traps, which appear to them to be a very attractive and cool resting place. About half an hour after completing the disturbance of vegetation and the "smoking" of surrounding buildings the doors of the trap are closed. Then the imprisoned insects are caught one by one in test-tubes (the traps being large enough for a boy to enter), or are simply killed by placing the trap in strong sunlight for an hour or two, by which time all the mosquitoes will be found lying dead on the floor of the trap. In a trap of this kind favourably placed in a garden in Colombo there were caught on an average 280 mosquitoes each day for a month during November and December, 1913.

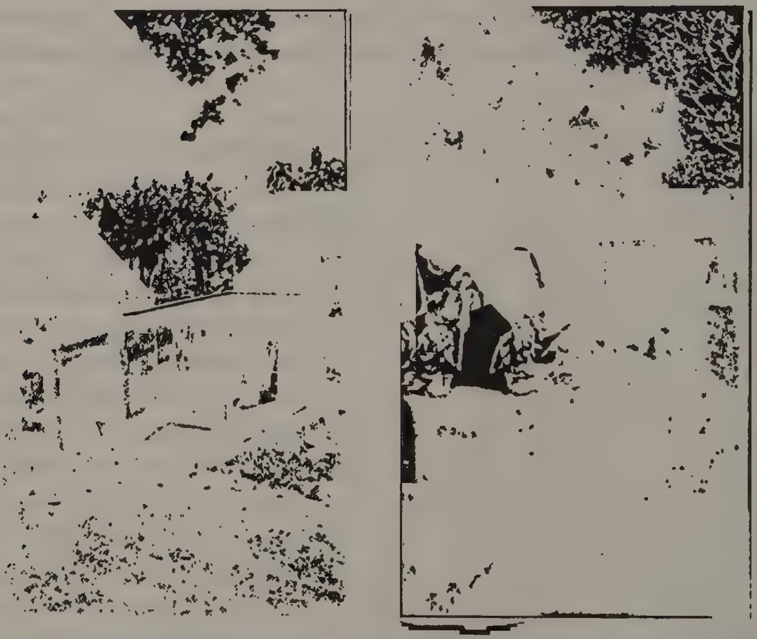

FIG. 50.—A trap for catching adult mosquitoes. The photograph on the left shows the trap not set; that on the right shows the same trap set as described in the text.

Distance of Flight and Mode of Spread in an Area.—In experiments to ascertain the usual distance of flight of particular species it is difficult to distinguish between the initial flights which may be of a migratory character and the short flights subsequently made for obtaining food and for laying eggs. Over the bare plains of Northern India half a mile is a common distance traversed by anophelines in their first flight and much longer distances have been recorded. The observations relate to: (*a*) Places in which all possible breeding places have been obliterated within a certain circumference from a town; (*b*) the appearance of mosquitoes on ships moored within a known distance from a port; (*c*) direct observation of mosquitoes in flight; (*d*) catching, staining and liberating anophelines at a given point and then recatching at given distances from a point of liberation. In the last method, when positive results are obtained, it is certain that the particular distance recorded has been traversed. The following is a summary of an experiment of this kind carried out by Geiger, Purdy and Tarbett in a rice field district in America.[1]

On August 27, 5,000 mosquitoes, all being *A. quadrimaculatus*, and about four-fifths being females, were caught. They were transferred to containers consisting of lantern chimneys of which the open ends were covered with mosquito netting. They were stained by spraying them with a 1 per cent. aqueous solution of methylene blue, the stain being sprayed from an atomizer of which the nozzle was inserted through the mosquito netting. Nine hours after catching, approximately 4,000 of the stained mosquitoes were alive and active, and they were liberated at dusk at the station marked 1 on the following chart (fig. 51). Sixty hours later recatching was commenced and was continued for seven days, the stations examined being marked 1 to 37 on the chart. The total number of mosquitoes caught during this period at the thirty-seven stations was 19,831, and they were examined by adding a drop of solvent (alcohol 3 parts, glycerine 3 parts, chloroform 1 part), to each mosquito placed on a microscope glass slide on a white background and examining with a lens. Ten stained mosquitoes were found in this way. Of these, nine had been caught at Station No. 10, which was three-fourths of a mile from the liberating point and one had been caught at Station 15, which was 1 mile from the liberating point.

The following are instances of direct observation:—

(1) In the Panama Canal zone in December, 1912, there was a sudden influx of anopheline mosquitoes at Gatun, the numbers of adult insects increasing until they were very much larger than had ever occurred previously. Thorough investigation of all breeding places made it probable that a fresh water swamp, part of which was 1,660 yards, and part 2,000 yards, from Gatun, was the source of the adults, and it was then decided to test the matter by actual observation of the adult insects which emerged so numerously from the swamp. The following is an extract from the record of these experiments:—

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[1] *Journal of the American Medical Association*, March 28, 1919, p. 844.

"On January 20, at 4.30 p.m., observers were posted on the side of the French Canal opposite to the propagation area, and they faced the latter to observe any marked flight that might occur. Previously to 6.20 p.m. practically no mosquitoes were noted. At that time birds of the kind that feed on flying insects appeared to be very active, and were apparently feeding on insects in the air at an elevation of 30 or more feet above the water surface. Later the birds operated at a lower elevation, and at about 6.30 p.m. were feeding at about 6 feet or less above the water. It was at this time that the observers on the bank and in the boat noticed the first appearance of anopheles. The flight was from west to east and quite marked. As it became darker the quantity of flying anopheles increased, and by looking past a dark object against the clear sky hundreds of anopheles could be seen passing by. These observations were continued for four consecutive nights, and the time of the start of the flight-period remained about the same. After dark the flight was markedly reduced and practically stopped completely before 9 p.m. . . .

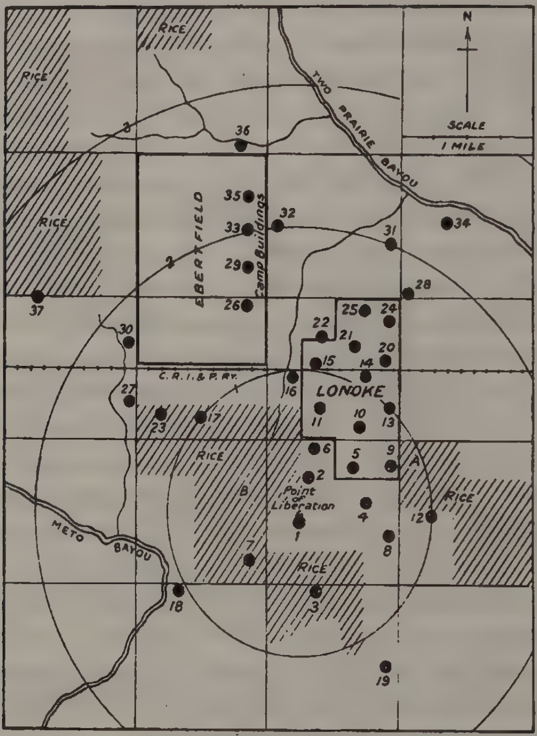

FIG. 51.—Location of Catching Stations. (See p. 72.)

Adult anopheles were stained with dye and liberated at the swamp. Subsequently some of them were collected on the opposite side of the river at the locks and in houses, 4,700 feet from the liberating station."

(2) In April, 1912, I had an opportunity of observing, from a ship lying at the mouth of the river below Guayaquil in Ecuador, a similar migration or flight of mosquitoes. The ship was lying, the captain informed me, about three-quarters of a mile from the shore. The evening was exceedingly wet and windy, but shortly after dusk mosquitoes began to arrive in such numbers as to make it almost essential to get under mosquito curtains. The mosquitoes included two species of anophelines and various culicines, but no member of the Stegomyia genus, and no *Culex fatigans*. It appeared to me that the ship had intercepted only a small proportion of a great swarm of mosquitoes that were making for the town of Guayaquil, about 1½ miles farther up the river.

Mosquitoes spread in an area not only by direct flight from extensive breeding-places, but also by a gradual infiltration. Not all newly hatched mosquitoes return to the house or village from which their parent came. Some of them reach houses in the opposite direction, and, having found food and a home there, proceed to breeding-pools still farther removed from the original village. Yet another method of spread is by being conveyed in ships, carts, railway carriages, &c.

Sheltering Places.—Some species of mosquitoes (e.g., *A. maculipennis*) pass most of their lives in buildings; others (e.g., *A. bifurcatus*) find shelter almost exclusively in undergrowth, shrubs, and vegetation in the open; others (e.g., *A. plumbeus* and *Stegomyia micropteron*) shelter chiefly in tree-holes. Mosquitoes which shelter in the open may very easily escape observation. Major Christophers found in the Punjab that such anophelines sheltered on the dry, sun-baked plain in small bushes, in tufts of tall grass, in a low scrubby plant somewhat like heather, and even in small depressions in the ground formed by sinking and cracks. In Colombo I found anophelines frequently in holes in an old wall in a garden, and in depressions on the ground. A good way to search for anophelines in these situations is to cover an area of ground with a large mosquito-net and then to enter the net and beat the ground vigorously with a stick. The dislodged mosquitoes which have flown up into the net can then be caught in test-tubes. In places where the undergrowth affords more shelter it is often sufficient to sweep it with an entomological net.

Time of Biting.—Anophelines are most active just after sunset and just before sunrise, but some species bite throughout the day. In Guayaquil (Ecuador) in 1912 anophelines could be caught very easily in the middle of the day by standing for a few moments in the main street of the town and putting a test-tube over them as they alighted on one's hand or arm.

Influences which attract Mosquitoes.—Next to the necessity of finding shelter against the sun and other adverse climatic influences and natural enemies, food supply is probably the factor which has most influence in determining the presence of mosquitoes in particular parts of a locality where they occur. They are seldom or never found in unoccupied houses, and the evacuation of a village leads almost at once to the departure of all the anophelines which formerly may have been abundant in it. To some species animals are even more attractive than human beings; and even human beings differ greatly from one another in relative attractiveness. Birds, and even frogs and reptiles, are quite attractive to some blood-sucking species. Experimental work does not give much support to the usual view that mosquitoes are attracted chiefly by their sense of smell, but Mr. Howlett has made some experiments which show clearly that radiant heat is very attractive to some species. In experimental work on this subject it is, of course, a mistake to proceed on the view that substances or circumstances which attract or repel human beings are likely to attract or repel mosquitoes.

The presence of suitable breeding places in the immediate neighbourhood is apparently a factor of only secondary importance; for it has been shown that where there is an abundant food supply anophelines will travel long distances to reach it, and will, when necessary, traverse an equally long distance to lay their eggs (Christophers).

Breeding Places.—The observation that certain species of mosquitoes select only certain kinds of collections of water in which to lay their eggs is an old one and of great importance to the practical sanitarian who desires to know what kinds of collections of water should be dealt with in an anti-larval campaign against a particular species. The habit, however, is much more marked in some species than others. The best examples of it occur among comparatively rare species, such as *Harpagomyia genurostris*, whose larvæ can be found only in the small collections of rain-water contained in the foliage of certain plants, and *Stegomyia micropteron* and *Anopheles plumbeus*, whose larvæ are found in narrow deep holes in the trunks of trees. Quite the reverse are the ubiquitous mosquitoes *Culex pipiens* and *Anopheles rossii*, which lay their eggs without selection in almost any collection of water that happens to be in their vicinity when their eggs are mature.

Stegomyia fasciata, the carrier of yellow fever, is a species which is highly specialized as regards its breeding places. It breeds almost exclusively in artificial water containers, of which nearly all are "man-made." The degree of preference of this species for man-made breeding places, such as household utensils, water-storage receptacles, roof gutters, &c., as compared with all the natural breeding places in which its larvæ may be present, was found in Colombo to be roughly as 92 : 8; and as compared with such important natural breeding places as swamps, pools, ponds and streams as 100 : 0. The kind of water is also almost always clear and free from mud; it is usually rain-water or the water of a public supply.

The adherence of the species to this habit is put to the test when all breeding places of the above kind are abolished from an area and their place taken by a number of "trap breeding places" containing water of the same character, the unfavourable breeding places in the area being left as they were. For *Stegomyia fasciata* the most effective trap breeding places are earthenware pots containing rain-water (fig. 52). The result of such an experiment is that all the trap breeding pots almost at once become heavily infected while the unfavourable breeding places still remain uninfected as was the case before the experiment was begun.

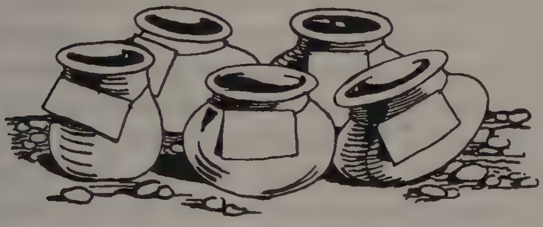

FIG. 52.

It should be noted here that the best way to search for larvæ in earthenware pots and other domestic utensils is first to empty most of the water and then, after stirring and shaking the vessel, to pour the remaining water through a piece of fine muslin or calico as is shown in fig. 53. The vessel should be rinsed with water several times (because the larvæ cling tightly to the sides and bottom) and then the calico strainer should be turned upside down into a dish of clean water in which the larvæ washed off the calico can be plainly seen.

FIG. 53.—Searching for larvæ by straining water from domestic water-storage vessels through muslin.

Anopheles stephensi often breeds in similar artificial water containers or in wells. *Armigeres obturbans* is a species which resembles *fasciata* in choosing to lay its eggs in artificial collections of water, but differs essentially in the kind of water that it prefers. This is almost always very dirty and often grossly contaminated with sewage or other animal contamination.

In marked contrast to these species which choose to lay their eggs in artificial collections of water, is a large group whose breeding places are almost entirely natural collections such as swamps, pools, ponds, grassfields and lakes. This group includes many species of anophelines. The water in such breeding places is usually stationary, but there are certain species of anophelines whose chief breeding places are irrigation canals and more or less swiftly running streams and rivers.

Anopheles turkhudi is a species whose breeding places in the Punjab in India are almost restricted to the beds of rivers; and *Anopheles listoni*,[1] an active malaria carrier, is chiefly a stream-breeding species. There is another group of species which breeds almost exclusively in holes in trees and shrubs. The English *Anopheles plumbeus* belongs to this group. Yet another mosquito with specialized habits as regards breeding places is *Anopheles ludlowii*, the larvæ of which are frequently found in salt water pools along a sea-beach. In some instances the water in which the larvæ of this mosquito have been found has contained a higher percentage of salt than ordinary sea-water.

These examples will be sufficient to indicate how necessary it is to study the breeding places of each species separately.

Probably the best general division of breeding places is that used by Dr. Bentley in regard to the breeding places in Bombay city. He divided them into

(*a*) Permanent.
(*b*) Temporary.

Permanent breeding places are specially important in countries liable to long periods of drought. Major Christophers enumerated the chief breeding places under these headings in the Punjab as follows :—

A. *Permanent :*
  (1) Large river beds like that of the Jumna.
  (2) Large sheets of water ("jheels" and "tanks") filled with aquatic vegetation and their associated swamps and pools.
  (3) Extensive brick fields and large excavations.
  (4) Irrigation systems.

B. *Temporary :*
  (1) Pits and excavations.
  (2) Shallow accumulations of rain-water.
  (3) Irrigation channels.
  (4) Miscellaneous sources.

During continuous rainy weather many collections of water which quickly dry up when the rains are light and intermittent become of great importance. At such times much undrained low-lying land becomes saturated with water which oozes out and collects in small depressions and pockets on the surface and forms numerous breeding places often quite hidden among grass and weeds. In this way whole fields and plantations become converted into areas on which it is necessary to do no more than scoop up a little mud and water in order to find many anopheline larvæ. In some districts a similar condition is produced by seepage water oozing from undrained slopes, and in such places larvæ can be found not only in actual pools but on the grass-grown land itself wherever it is sufficiently saturated to enable a teaspoonful or two of water to be collected.

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[1] In the synoptic tables *Anopheles listoni* is named *Anopheles funestus* variety *listoni*.

Other Egg-laying Habits.—Anophelines and a few other kinds of mosquitoes, which lay their eggs one by one, seldom lay all the eggs of a generation on the same collection of water, but usually lay a few on one collection, a few on another, a few on a third, and so on, sometimes infecting in this way four or five collections of water with eggs from the same batch. This habit gives these species an advantage over mosquitoes whose eggs of the same generation are joined together in the form of a raft and therefore must all be laid on only one collection of water.

Mosquitoes, when laying their eggs, must rest on the ground or on some object which affords a firm foothold. For this reason the eggs are laid as often as not on the damp mud near the water's edge instead of on the water itself. Eggs so laid can withstand a considerable degree of drying and retain their viability for a long time. They hatch into larvæ when a shower of rain fills the pool sufficiently to float them off the mud.

Adult female mosquitoes drink water freely and they usually do so before laying their eggs. Some species are much more particular in regard to the kind of water which they will drink than others, and this may account, in part, for the varied selection of breeding places by different species.

GROUPING OF SPECIES ACCORDING TO HABITS.

On the above and other characteristic habits it is usually possible in any place where mosquitoes are very prevalent to group the different species according to habits as follows:—

A. Urban Mosquitoes.
    Group 1. The strictly household species.
    Group 2. Other urban species.
B. Rural Mosquitoes.
    Group 3. Strictly sylvan species.
    Group 4. The migratory species.
    Group 5. Species with peculiar or unexpected habits.

Recorded as briefly as possible the following are characteristic habits of the mosquitoes in each of these groups:—

Group 1. The strictly household mosquitoes live in intimate association with man and his dwellings. Their breeding places are of a particular kind found in the environment of human beings only: and their whole life is spent within, or in the immediate vicinity of, the house in or near which they were born. *Stegomyia fasciata*, the carrier of yellow fever, is the best example of this group.

Group 2. These are not so closely dependent upon man as are the mosquitoes of Group 1, but they pass the whole of their lives in one or other section of a city or town, seldom leaving the vicinity of the place where they were born. They are able to breed in almost any kind of water. *Culex fatigans*, the carrier of filariasis and of dengue fever, is the best example in this group, and perhaps the common English mosquito *Culex pipiens* (which in appearance closely resembles *fatigans*) may be another example.

Groups 1 and 2 include all mosquitoes usually called "domestic mosquitoes."

Group 3. The strictly sylvan species spend all their life in a rural environment usually far from towns. They do not visit houses.

Group 4. The so-called "migratory" species, while retaining their habit of breeding in swamps and natural pools at a distance from centres of population, have the habit of flying long distances into towns for the purpose of obtaining meals of blood. In the tropics this group contains a good many species of *culicine* mosquitoes, and, unfortunately, several *anophelines;* but whether any of the English mosquitoes have the habit of making long flights from their breeding places is not yet known. In a district where anti-mosquito operations are being conducted, the presence of migratory species is very disconcerting, because their sudden and unexpected influx into an area causes the residents to believe that the local operations have failed.

Group 5. So far as is known at present, no English mosquito is likely to be found in this group, which in the Tropics includes certain species that have not the power of biting through the skin nor of sucking blood. One species, *Harpagomyia genurostris*, has the very curious and interesting character of living in close association with ants, which supply it, from their mouths, with honey that they have collected.

CHAPTER V.

A Malaria Survey and Some Epidemiological Observations in England.

We have now reviewed most of the technical methods and epidemiological observations with which those who carry out public health inquiries into malaria should be familiar. These inquiries are usually called " Malaria Surveys," and are understood to include all the practical field and laboratory work necessary for obtaining in any locality sufficient information of the occurrence, mode of origin, and spread of malaria to enable a definite plan for dealing with the disease to be drawn up.

In its simplest form a malaria survey does not differ from an epidemiological inquiry into the occurrence, origin and spread of any other infectious disease; and because we know that malaria is conveyed from person to person in only one way, and can be detected in both the human source and the insect carrier, the procedure of the inquiry is often more straightforward, and the results which emerge usually give a clearer indication of the correct measures to adopt, than is the case with some other diseases. In its essential features a malaria survey is concerned with :—

(1) Confirming or discovering the occurrence of the disease in the locality and ascertaining its distribution, amount and character.

(2) Searching out the human sources of infection and ascertaining their condition as hosts of the parasite and their circumstances in relation to the insect carrier.

(3) Ascertaining the particular species of mosquito which is transmitting the disease and the degree to which it is infected (sporozoite rate), and obtaining a complete knowledge of its life-history in the locality and its habits in relation to the human sources of infection and the susceptible population.

(4) Studying any circumstances of the susceptible population which tend to favour their infection.

(5) Ascertaining what conditions in the environment favour the spread of the disease, having regard to both the human population of the locality and the insect carrier of the disease.

(6) Correlating the results of the above observations with the object of drawing a clear picture of the amount, distribution and character of the disease and especially of the manner in which it has arisen and is spreading in the locality.

(7) On this statement formulating a precise plan of action which, with a knowledge of the financial and other circumstances of the locality, will be a plan which it is practicable to carry out.

The subject stated in the last of these headings is highly important and often very difficult. On the first and every day throughout the inquiry it should be kept constantly in view. The observer who neglects its early and continuous study may write an excellent epidemiological report, but he may sometimes fail to place before the administrator of the locality a plan which, while offering a reasonable prospect of success, can be applied with the means available.

During and since the war the occurrence of cases of locally contracted malaria in England has provided opportunities of carrying out a number of small malaria surveys in which it has been possible to trace very clearly the origin and mode of spread of the disease, and as a result to state with precision the method which should be adopted for preventing the further occurrence of new cases. A brief account of one of these inquiries will be a suitable introduction to the more extensive surveys which are necessary in malarious places in the Tropics, and will give an opportunity of recording information on the epidemiology of malaria in this country.

A MALARIA SURVEY IN ENGLAND.

On August 21, 1917, at the Manor War Hospital, Epsom, benign tertian malaria parasites were found in the blood of a soldier who had never been out of England, and whose history showed that in all probability he had contracted the infection at a military camp near Sheerness, in the Isle of Sheppey. Arrangements were therefore made for a malaria survey of the camps and civil areas in that district.

For the purposes of a preliminary inquiry we proceeded to Sheerness on August 28, carrying with us sufficient apparatus for taking and examining blood-films, and for catching, dissecting, and examining mosquitoes.

On arrival at Sheerness our first work was to confirm the view that locally contracted cases of malaria were occurring. To do so we first examined all the cases with symptoms suspicious of malaria which were under treatment in the military hospitals of the area. The examination of blood-films from these patients showed that malaria parasites were present in the blood of six men who had never been out of England, and of three who had never been farther than France. We failed to find parasites in some other patients whose signs or symptons did not differ from those of the cases in which parasites were present, but this negative result was due, in all probability, to quinine treatment having been begun prior to our visit.

We next visited the different camps in which the hospital patients had lived, and made arrangements to examine and take blood-films from all men who appeared anæmic or complained of being "out of sorts," but not ill enough to cease duty. These examinations led to the discovery of several more cases among men who had never been out of England.

During a visit to one of the camps our attention was drawn to similar cases of illness among civilians living near the camp. We visited these patients and found malaria parasites in two who resided in the vicinity of the camp and in two who resided in Queenborough town, which is a few miles from Sheerness. One of the civilian patients was a boy 12 years old, and none of them had ever been out of England. The infection in all cases was with the benign tertian parasite.

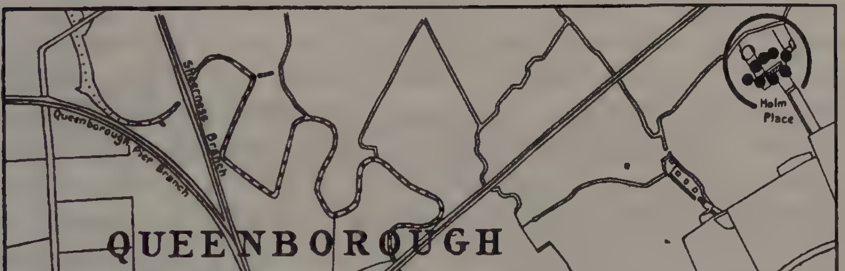

FIG. 54.

The results of this part of the investigation proved that an outbreak of locally contracted malaria of the benign tertian type was occurring in the area and that it had affected the civilian inhabitants as well as the troops.

Extent of the Outbreak.—An examination of the hospital statistics, in the light of the findings recorded above, showed that about seventy cases which in all probability were malaria had been admitted to hospital during the three months prior to the inquiry. In one regiment thirty cases which are now known to be locally contracted malaria, occurred during August.

Season and Duration of the Outbreak.—From the hospital statistics it appeared probable that cases had been occurring since June. The number of cases rose to a maximum about the end of September.

Localities of the Outbreak.—The chief foci of infection are shown on the preceding sketch (fig. 54).

The Human Sources of Infection.—(*a*) Among the troops who returned from Salonika to the depot of their regiment at Sheerness relapses of malaria contracted in the Struma Valley had been occurring since April, 1917. Nine such cases were admitted into the Sheerness Military Hospital in April, five in May, seven in June, seven in July and four in August. Malaria parasites were found in the blood of some of these men while they were in the camp, and there is no doubt that they were the original source from which anopheline mosquitoes in the camp became infected. (*b*) During the investigation of civilian cases in Queenborough town one or two cases were found which could not be ascribed with probability to an origin from military foci, and it was ascertained that at least one of them had originated before troops began to return from Salonika. On these findings and with the local knowledge that as late as 1865-70 "nearly everyone in Queenborough suffered from ague," it appeared probable that some of the civilian cases might be examples showing that the true indigenous disease had never entirely disappeared from the town.

The Insect Carrier of Infection.—Our visit was made during a period of high winds and rain, but despite these unfavourable conditions we found adult *Anopheles maculipennis* without difficulty in the huts occupied by the troops and they were present in great numbers in the bedrooms of two of the civilian patients and in civilian outhouses and cowsheds close to the camps. They were indeed prevalent throughout the district, and on August 30, during a search lasting not more than fifteen minutes I caught nineteen in the bedroom of another civilian patient in Queenborough town. Their larvæ were abundant in ponds and ditches near the camps and in numerous other collections of water in and around Queenborough and Sheerness. The following photograph (fig. 55) illustrates a flooded area in which they were particularly numerous.

Inquiry to ascertain the Sporozoite Rate.—I dissected forty-two adult female *Anopheles maculipennis* which had been caught in infected bedrooms and huts, but found no zygotes or sporozoites. It would, however, have been only a fortunate chance to find an infected specimen among so small a number, and since *A. maculipennis* was the only species of anopheline present in the locality and was obviously living in close association with human beings, there was no doubt that this species was the carrier of the disease. On returning to our laboratory at Epsom I carried out feeding experiments which demonstrated conclusively that the species is an efficient host of the benign tertian parasite in this country.[1]

Fig. 55.

Summary and Recommendations.—The above were the chief results obtained during the preliminary inquiry which lasted four days. They were sufficient to justify a report advising prompt action, for it was clear (*a*) that there was quite a considerable outbreak of locally contracted malaria affecting both troops and the civil population in the area, (*b*) that among both classes of people there were cases in which the nature of the illness had been unrecognized, (*c*) that human sources of infection in the persons of returned malarious soldiers existed almost throughout the area, and (*d*) that the insect carrier of the disease was everywhere present in great abundance, and in close association with the human sources of infection and the susceptible population.

The plan of action recommended was on the following lines:—

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[1] See *Journal of the Royal Army Medical Corps*, November, 1917, p. 615.

(*a*) *As regards the Troops.*

(1) The measures should be placed under the supervision of a specialist sanitary officer who has experience of malaria.

(2) In the peculiar conditions of the area (which is below high tide level, and very marshy) it could not be hoped that an endeavour to reduce the prevalence of mosquitoes would be successful within a period which would affect the present outbreak, and the task would require much labour which at that time could ill be spared. Moreover it was clear that in this instance quicker and surer results were to be expected from a campaign directed against the human sources of infection (which were comparatively few and localized) than from a campaign against the insect carrier which is ubiquitous and extraordinarily numerous. The chief effort, therefore, should be concentrated at once upon dealing with the sources of infection by a campaign of detection, segregation and quinine treatment.

(3) The methods to be adopted for discovering all men who might possibly be sources of infection and the arrangements for their segregation in mosquito-proofed huts, their systematic daily treatment with quinine and their transfer when necessary to special hospitals outside the area were then described.

(4) Three additional measures were recommended with a view to stop the occurrence of new cases from mosquitoes which had already become infected, and to minimize the results of any infections which were in the incubation period at the time of the inquiry. These were: (1) the evacuation of a building in which several cases had arisen and a subsequent endeavour to rid it of all the infected mosquitoes which it apparently harboured; (2) an attempt each day to rid the huts of all the adult mosquitoes which were hiding in them; (3) prophylactic quinine parades for all men in the infected areas of the camps.

(*b*) *As regards the Civil Population.*

For the civil population, as for the military, the action recommended was based on an endeavour to discover and control cases and carriers as early as possible. For this purpose it was suggested that the notification of malaria should be made compulsory and that this should be supplemented by arrangements for personal inquiries and the taking of blood-films in households and schools. The action to be taken when a case or carrier was discovered by any of these means was described.

FURTHER OBSERVATIONS ON MALARIA IN ENGLAND.

I shall now refer briefly to some of the observations on malaria in England which were made by different workers subsequent to the above inquiry.

Continuing first the story of the disease in Sheppey, the important observation was made by Lieut.-Colonel Wilkinson, who continued the survey among the civil population on behalf of the Local Government Board, that in England, as in the tropics, the examination of school children is one of the most valuable means of ascertaining the existence and prevalence of malaria in a locality. On October 28, 1917, he inspected all the children in the elementary schools of the Queenborough Urban and the Sheppey Rural Districts and took blood specimens from thirty-eight children who were anæmic or in poor condition. Benign tertian malaria parasites were found in the specimens from four of these children (10·5 per cent.), thus indicating a quite considerable occurrence of locally contracted malaria in the area.

Next it was found that some of the locally contracted cases among adults in Sheppey were of so mild a type that in the absence of personal inquiry from house to house and the taking of blood-films they could have remained undetected. In Queenborough town, at the beginning of 1918, there were eleven residents who had been discovered or notified as having contracted malaria during 1917. Dr. Seelly, who had been appointed Special Malaria Officer on the civil side, kept these cases under continuous observation and in April and May, when several of them suffered from relapses, they were provided with medical attendance and treatment and with mosquito curtains free of cost. When these arrangements became known, several other persons, whose cases had not previously come to notice, reported themselves to Dr. Seelly, so that by the end of May, 1918, the number of known cases in Queenborough had risen to eighteen. Systematic house-to-house inquiry for cases and the taking of blood-films were then begun, with the result that by the end of the year the total number of malaria patients known in the town amounted to thirty-two, of whom it was believed all except five had their first attack in 1917 or previously.

MALARIA AND ANOPHELES IN QUEENBOROUGH, 1918.

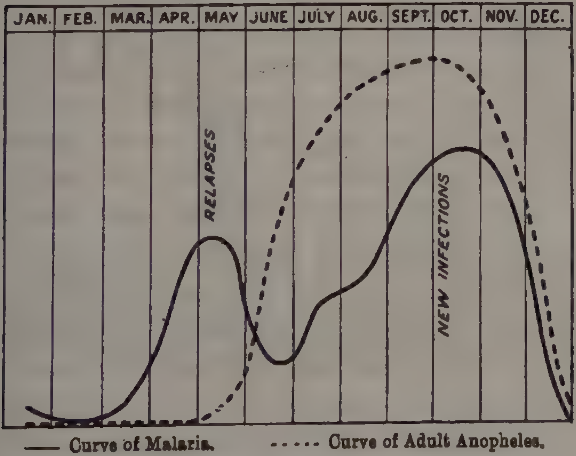

Fig. 56 - Malaria and anopheles in Queenborough, 1918.

Relapses and the Seasonal Incidence of Anophelines.—Among twenty cases of locally contracted malaria in Queenborough which were continuously observed since their original attacks six had no relapse during 1918, and among the remaining fourteen cases there were nineteen relapses, of which three occurred in April, seven in May, four in July, four in August, and one in September. Careful search failed to reveal the presence of any adult anophelines in the houses during April and May when most relapses occurred. During the first week of June a few male and female adults of the first brood were found in stables, but the number increased slowly and it was not until July 18th that adults were first found in dwelling-houses in the town. The chart drawn in fig. 56 above indicates roughly the malarial and anopheline curves in Queenborough town during 1918.

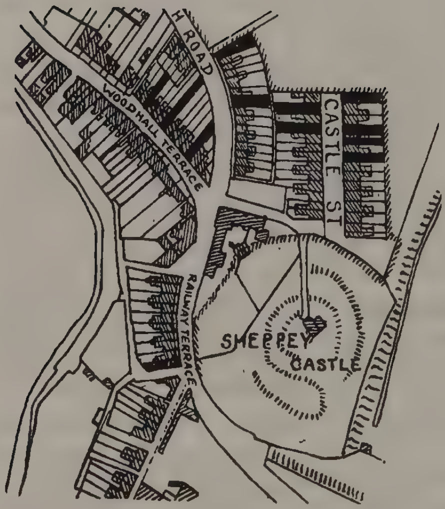

Fig. 57.

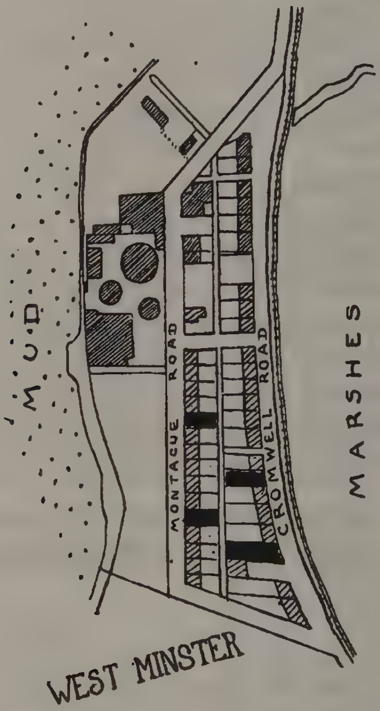

Fig. 58.

Indigenous Malaria in England is a Disease of Households or Families.—In Queenborough town the cases of indigenous malaria were not scattered in a random manner throughout the town but were definitely localized to certain streets and houses. Most of them were in the three groups which are ringed on the sketch map reproduced on p. 82 (fig. 54). In H—— Street there were cases in the houses numbered 19, 27 and 29; in C—— Terrace in the houses numbered 1, 4 and 6; in W—— Terrace in those numbered 2, 5 and 12; and in C—— Street in those numbered 20, 24, 25, 26, 27 and 32. The relative situation of the affected houses in one of the groups (C—— Street and W—— Terrace) is shown in fig. 57 above and the relative position of the affected houses in a group at the village of West Minster in fig. 58.

The localized character of the distribution is more clearly indicated by the incidence in particular houses; and on this subject the findings provided some striking examples of "malarious houses" quite comparable to the well-known instances of "yellow fever houses" which were such a puzzle to epidemiologists before yellow fever was known to be carried by the domestic mosquito *Stegomyia fasciata*. In No.— C—— Street there were five cases at intervals; in another house there were three cases, and in four houses there were two in each. In the first of these houses the occurrence of cases at intervals suggested the need of a blood examination of all the occupants. This was done and the landlady was found to be an apparently healthy carrier of malaria parasites. Unknowingly, she was probably the original source of infection to several lodgers in her house. Major A. C. Parsons has recently investigated in other localities in England a number of similar cases in which demobilized soldiers have been the source from which various members of their families or visitors in the houses have contracted the disease. The following are a few examples: (1) At Bobbing near Sittingbourne a demobilized soldier, since his return from Salonika in January, 1919, has lived at home and had many relapses of fever. In the middle of September his wife and two children contracted the disease. (2) At Great Ryburgh, Norfolk, in October, 1919, a little girl aged 7, was attacked with malaria, her blood showing a very heavy infection with *P. vivax*. Her father, a discharged soldier, has had many relapses since his return home five months ago, and on October 15 his blood was found to contain many parasites, including gametocytes. (3) At Wivenhoe Cross, Essex, a schoolboy was attacked with a rigor while at school on October 2, 1919, and he afterwards went through a typical attack of benign tertian malaria. It was found that he had been sharing a bed with an elder brother who suffered very severely from malaria while in the Army, and has been having attacks repeatedly since his return home.

The localized character of the distribution of cases of malaria in England, and particularly the incidence in houses and families, indicates that the mosquito concerned (*A. maculipennis*) has the habit of remaining most of its life within or in the immediate vicinity of the house where it obtained its first meals of blood.

GENERAL REVIEW OF LOCALLY CONTRACTED MALARIA IN ENGLAND DURING 1917 AND 1918.

The inquiries in the Queenborough and Sheerness area have been referred to in some detail as being the first moderately full survey on modern lines made in this country. Similar, and in some instances more complete, inquiries have since been made in other parts of England, and the steps taken by the Local Government Board and the Ministry of Health providing for compulsory notification of cases throughout the country and for inquiry into all cases of indigenous origin have yielded valuable information. The subject has also been closely studied in the Navy and Army. The following notes are summarized chiefly from the published "Reports to the Local Government Board," to which reference has already been made.

Incidence in 1917 *and* 1918.—The total number of locally contracted cases notified or discovered by special inquiry from September, 1917, to the end of 1918 were 330, of which 38 were in the Navy, 224 in the Army and 68 in the civil population. So far as information is available, the following is a record for each of the two years of the localities in which cases were detected and the numbers reported in them among the Navy, Army and civil population respectively.

County	Place	Navy		Army		Civilians	
		1917	1918	1917	1918	1917	1918
Kent	Sheerness and Sheppey	6	3	68	31	35	14
	Isle of Grain	14	5	3	3	—	7
	Sandwich	—	—	69	6	1	1
	Lydd	—	—	1	2	—	—
	Chatham Area ..	1	—	—	—	—	—
Essex	Tilbury	—	—	—	—	3	—
	Walton-on-Naze ..	—	—	—	—	2	1
	Dovercourt	—	—	—	3	1	1
	Purfleet	—	—	—	1	—	—
Surrey	Walton-on-Thames ..	—	—	2	—	—	—
Dorset	Parkstone	—	—	—	1	—	—
Suffolk	Southwold	—	—	—	—	1	—
	Bawdsey	—	—	—	3	—	—
	Shotley	—	1	—	—	—	—
	Felixstowe	2	—	—	—	—	—
Norfolk	Thetford	—	—	—	2	—	—
Sussex	Uckfield	—	—	—	1	—	—
Lincolnshire ..	Tetney Lock	—	—	—	1	—	—
	Grantham	—	—	2	—	—	—
Leicestershire ..	Leicester	—	—	—	1	—	—
Nottinghamshire	Chilwell	—	—	—	1	—	—
Salop	Shrewsbury	—	—	—	—	—	1
Hampshire ..	Aldershot	—	—	4	4	—	—
	Southampton.. ..	1	—	—	—	—	—
	Portsmouth	1	—	—	—	—	—
Hertfordshire ..	London Colney ..	—	—	—	1	—	—
Elsewhere ..	—	4	—	14	—	—	—
	Totals	25	9	163	61	43	25

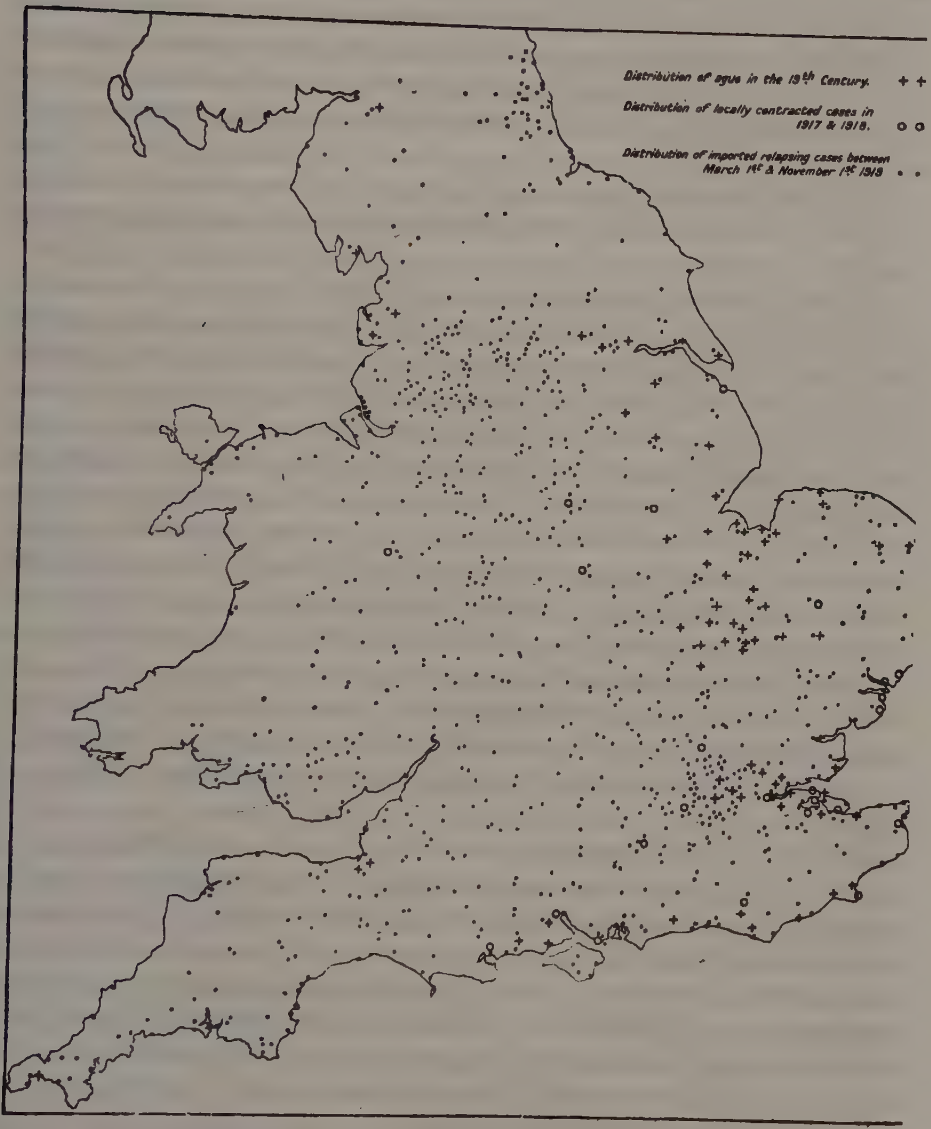
Distribution of ague in the 19th Century. + +
Distribution of locally contracted cases in 1917 & 1918. o o
Distribution of imported relapsing cases between March 1st & November 1st 1918 • •

FIG. 59.—Map of England showing distribution of malaria.

It will be seen that a case or cases of malaria of indigenous origin occurred in a number of widely separated places, but that in only one county (Kent) was there a considerable local spread of the disease. Available information does not suffice to explain the exceptional incidence in this county, but it is of particular interest that it is the only county in which evidence has been obtained which indicates that there remain a few areas in England where endemic (true indigenous) malaria still persists.

Local Distribution of the Cases.—This subject (in connection with which the occurrence of multiple cases in particular houses is of chief interest) has already been mentioned on p. 87.

Seasonal Incidence.—According to the Naval and Military returns of new cases in 1918 about 85 per cent. of the cases were detected during August and September, but there are records of a few new infections as early as May and as late as October. In 1918 an infection in May or earlier must have been due to an anopheline which had lived through the winter, for in that year the first brood of new adult anophelines did not appear until quite the end of that month. The particular anopheline concerned might have become infected in the previous autumn and lived through the winter with sporozoites in its salivary glands, or, as was suggested by Captain Macdonald, R.A.M.C., it might have been wintering in an artificially heated room occupied by a malaria carrier. If in any particular instance the findings would not justify an appeal to either of those hypotheses it would be necessary to include an early case of this kind among the examples of infection in the previous year, the results of which remained latent till the spring. Several such cases of "latency" came to notice in 1918, and it appears that the observation was not uncommon in the early years of last century when ague was generally prevalent in some parts of England.

The Type of the Disease.—All the locally contracted cases of malaria so far reported in this country have been infections with the benign tertian parasite (*P. vivax*). It may be noted, however, that in France in addition to the commoner benign tertian infections a few new infections with the malignant tertian parasite (*P. falciparum*) have occurred. Dr. E. Roubaud has shown in Paris that *Anopheles maculipennis* is an efficient host of this parasite at temperatures which are usual during the summer in England. For these reasons, and in view of the large number of crescent carriers among returned soldiers, we cannot regard as negligible the risk that cases of this type may occur.

Clinically, the great majority of the English cases presented in a typical manner the characteristic signs and symptoms of "tertian ague," with paroxysms coming on at approximately the same time every other day. Some of the patients in their primary attack were laid up for a fortnight or more, and afterwards suffered from severe anæmia, but this and enlargement of the spleen (which was frequently considerable) were the only noteworthy complications reported. No death occurred. A few cases in Queenborough town were so mild in character that periodic attacks of "chilliness" or "slight shivers" were the only indications of illness. These cases were discovered by taking blood specimens during routine house-to-house inquiries. In an account of the civilian cases of malaria in Kent it is suggested, on epidemiological and other evidence, that possibly they might be infections with a true indigenous strain of the benign tertian parasite instead of with the apparently more virulent strain recently imported from Eastern war areas.

Relapses.—Most of the patients infected in 1917 suffered from a relapse within a month or six weeks after their primary attack, but from October relapses became very rare until April and May, when there was a noticeable increase in their number. The tendency of the indigenous disease to relapse at that period of the year led to the discovery of some cases which had previously escaped notice. During the early years of last century the occurrence of a spring relapse was apparently sufficiently characteristic to be of popular concern, for it is recorded that in South Essex polite inquiry into anyone's state of health often took the form: "Have you had your ague this spring?"

In all the cases infected in this country, relapses have been less frequent and less severe than is usual in cases of malaria contracted in the tropics.

Sources of Infection.—(1) The sources of infection of all the Naval and Military cases and of nearly all the civil cases which have occurred since 1916 have been relapsing cases of malaria among returned soldiers. Unfortunately, although each relapse of malaria in these men can be quickly cured by quinine, no treatment at present known suffices to effect a permanent cure within a reasonably short period. And although the arrangements made by the War Office and the Ministry of Pensions for the treatment of soldiers before and after demobilization tend greatly to reduce the frequency and severity of relapses, it is the case that many soldiers were demobilized who had recently had parasites in their blood, and that many ex-soldiers continue to suffer frequently from relapses in which they are capable of infecting the local anophelines and so spreading the disease. Since March 1, 1919, when the Ministry of Health's Malaria Regulations made notification compulsory throughout England and Wales, some 14,000 demobilized soldiers have been notified as suffering from relapses. The localities from which these notifications were received between March 1 and November 1, 1919, as well as the distribution of locally contracted malaria are shown on the map on p. 90.

(2) From the investigations in the Isle of Sheppey and from more recent investigations in the Isle of Grain, it is concluded that in these localities, and perhaps in one or two other localities in England, the sources of infection include

civilian cases of endemic (true indigenous) malaria as well as imported military cases.

(3) At certain English ports a potential source of infection of considerable importance is provided by the crews and passengers of transports and merchant ships from Dakar, Sierra Leone and other ports on the West Coast of Africa. During the war malaria was exceptionally prevalent and severe in those ports, one result being to introduce every month into the ports of London, Liverpool and Bristol between fifty and sixty sailors who a few weeks previously had become infected with malaria and had suffered severely on the voyage home. It has been ascertained that in this way during 1917 more than 500 cases of malignant tertian malaria were introduced into England from the West Coast and the Cameroons.

The Insect Carrier.—This subject has already been referred to in sufficient detail.

An Important Epidemiological Factor.—Consideration of various observations in connection with the human sources of infection and the insect carrier in England suggests that the factor which determines whether new cases of malaria will or will not occur in a potentially malarious locality in this country, and the extent to which the disease will spread, is neither the abundance of anophelines in the locality generally, nor of carriers, but is the degree to which there is close and continuous association between the malaria carriers, the anophelines and the susceptible persons. It appears that in this country the requisite degree of close and continuous association occurs only in particular types of dwelling which *A. maculipennis* selects as its permanent resting and feeding place. In practice such dangerous dwellings can be detected by ascertaining whether specimens of *maculipennis* can be caught in them day after day for a week or more during the season of their prevalence in the locality: and it is clear that it would be a wise precaution in places where examples of family infection have occurred to search out all such "malarious houses" and to prevent demobilized soldiers who suffer from relapses from occupying them.

CHAPTER VI.

A Malaria Survey and Some Endemiological and Epidemiological Observations in the Tropics.

A Malaria Survey in the tropics is always a more difficult and laborious task than such a survey as was described in the last chapter. In that instance it was possible, without any real difficulty, to ascertain the particular individuals who were sources of infection, and to trace the actual spread of the disease from case to case until a condition of epidemic prevalence resembling that of any other infectious disease had been attained. But in malarious places in the tropics a condition of almost universal infection has usually existed "from time immemorial"; and what we have to study is not so much the special problem of the exact origin and mode of spread of new cases, as the general problem of the conditions which tend to maintain a high degree of endemic incidence which may be producing serious effects on the birth and death rates, the working capacity, and the general welfare of the population. Such studies are correctly referred to as inquiries into the ENDEMIOLOGY of malaria.

In some malarious localities the amount of endemic malaria remains at about the same level throughout the year; in others the curve shows, each year, a wave of greater prevalence at a definite season, which is usually just after the rains. In the north of India (the Punjab) the wave is autumnal, but in the far south (Ceylon) it occupies the period from November to March. This periodic wave of enhanced prevalence is properly referred to as "the annual epidemic rise of endemic malaria," or shortly as "the annual epidemic." In normal times the degree of the rise is fairly constant from year to year. It has to be studied as an important item in the *endemiology* of the disease. The use of the term "epidemic" in that connection must not be confused with its use in the term EPIDEMIC MALARIA. This term is applied to certain remarkable outbreaks of malaria which at irregular intervals fall suddenly and with devastating effect upon extensive areas of country, including localities of high endemic incidence and localities previously almost free from the disease.

In addition to endemic and epidemic malaria, a third type, to which Major Christophers has given the name INCIDENTAL MALARIA, has to be studied. It is defined as "the type which affects the European or other immigrant population in an endemic area where the indigenous inhabitants, although they are the cause of the trouble, appear themselves to suffer little from the effects of the disease." This is the type which so seriously affected our troops operating in Macedonia and other Eastern war areas.

Perhaps the most important matter which should be realized in connection with surveys of endemic malaria in the tropics is that in practice such inquiries almost always necessitate what is really a detailed social, sanitary and economic survey rather than an exclusively malarial one. It is unwise to take any less comprehensive view of the subject than this, or to hope that a practicable plan for ameliorating the malarious conditions can be formulated from an inquiry in which, after ascertaining the amount and distribution of malaria in the locality, attention is chiefly concentrated on studying the insect carrier and the collections of water in which it breeds. Those are, of course, highly important details of the survey, but it is easy to spend too much time upon them and too little upon factors which superficially may seem to be far removed from the stated problem but, in reality, are at its roots. Some important social, economic and environmental factors have already been mentioned on pp. 15 to 17 of Chapter II, and the need of close inquiry into subjects of this kind will be clearly seen from the summary of an actual survey which follows.

Before giving that example of a malaria survey in a tropical area opportunity may be taken to note the methods usually employed for ascertaining the amount of endemic malaria present in tropical districts where the indigenous inhabitants show few typical symptoms of the disease and where there are no reliable arrangements for recording the causes of sickness and death.

Statistics.—Usually in the tropics the only community statistics which are sufficiently accurate to be utilized with advantage are those of the population and of the total births and deaths. If these are used with care, not as true figures, but as an index for comparison with other communities, and for ascertaining seasonal and annual changes, much useful information can be obtained from them.[1] If it happens that there is a hospital or dispensary in the locality, the diagnoses recorded in its books will give a rough indication of the prevailing diseases and their seasonal incidence, and a clue to the causes of any marked rise in the weekly or monthly deaths. The statistics of sickness and mortality among British and native troops who may be stationed in the locality also provide useful information, and can be correlated with the results of blood examinations made upon groups of the indigenous population each month throughout the year.

Personal Examination of the Inhabitants.—It will be obvious that theoretically the correct way of obtaining accurate information on the amount and distribution of malaria in a locality is to proceed from house to house and school to school making inquiries and clinical examinations and taking blood-films until practically all the inhabitants have been seen. On behalf of the Ministry of Health, Dr. A. C. Parsons has recently carried out a complete inquiry in that manner in a locality in England, but in the tropics this is seldom or never practicable. As a substitute for it various plans of "sampling" have been devised, of which the following are most frequently adopted :—

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[1] See *Paludism*, No. 1, July 1910, "Suggestions on the use of available statistics for studying malaria in India" by S. R. Christophers.

THE SPLEEN RATE.—In villages in the tropics it is seldom difficult, after the objects of the inquiry have been carefully explained to the people, to collect thirty or forty children who by the distribution of sweets or coppers can be persuaded to submit to clinical examination with a view to ascertain the presence and degree of splenic enlargement. The examination should be carried out as thoroughly as circumstances permit, but it has nearly always to be made while the child is in the erect posture. The age of the child should be ascertained as nearly as possible and the size of the spleen should be stated as being one, two, three, &c., fingers' breadth below the costal margin. Major Christophers adopts the following grouping, which also gives his estimations of the weight of the spleen during life in each group :—

Clinical finding	Group	Weight*
Spleen only just passes beyond the costal margin	1 finger's breadth	100 grammes
Spleen palpable below the ribs; so much can be inserted	2 fingers' breadth	150 ,,
Notch apparent at the costal margin	3 ,, ,, ...	200 ,,
Splenic edge above the notch can be felt	4 ,, ,, ...	400 ,,
	Hand breadth	500 ,,
Spleen reaches to umbilicus	To umbilicus	750 ,,
Spleen reaches to pubis	To pubis	1,000 ,,

* Weight of a normal spleen in a child = 50 grammes.

Fig. 10 on the next page illustrates roughly the size of the spleen in some of the above groups.

The term *spleen index* is used to denote the percentage of children between the ages of 2 and 10 years who have enlarged spleens due to malaria, but in field work it is best not to limit the examinations to children of those ages, but to examine all people, both children and adults, who will permit it. It is often quite as important to know the adult spleen rate in a community as it is to know the rate in children.

Before utilizing splenic examination as a means of estimating the proportion of people who are affected with malaria in a community, it must, of course, be ascertained that malaria is the disease responsible for the prevalence of enlarged spleens in the area. The method is not applicable in districts affected with kala-azar.

The Parasite Rate.—It is not possible to ascertain accurately the amount and kind of malaria prevailing in a community without taking and examining blood films from as many of the indigenous inhabitants as can be persuaded to allow their fingers to be pricked for the purpose. Native children who will submit to palpation for splenic enlargement seldom or never object to a film of finger blood being taken at the same time. The slides should be ready beforehand in a numbered slide-box and, (if the climate is moist) it is advisable to warm them over a spirit lamp just before use. Two or more needles should be available so that one may be rubbed clean and dry by the assistant while another is being used. Except these details it is best to have as little apparatus as possible, and as regards cleansing the child's finger to be content with a "dry rub" with a handkerchief. The drop of blood should be spread evenly with the needle according to the directions given on p. 21 (Chapter III), and after the film has been dried rapidly, the slide should be put away at once into its numbered groove in the box, so that it may not be soiled by dust and flies. The numbers opposite the grooves in the slide-box should correspond with the numbers in a note-book in which an assistant writes down the name, age, size of spleen, &c., of the person examined. Films of *at least* twenty-five children should be taken and it is always advisable to take films from as many more as can be obtained. Great care should be taken that the slides are well and correctly stained, and the worker who examines them should have had considerable experience in detecting skin organisms, yeasts, &c., which may bear a superficial resemblance to malaria parasites.

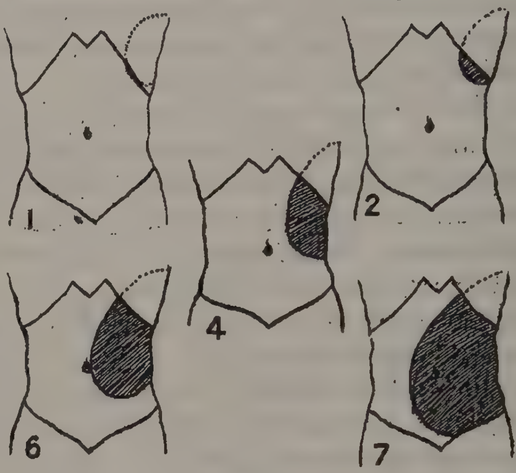

Fig. 60.

Before recording a film as "negative" the number of microscopic fields examined should be not less than 200. (See also the remarks under "Diagnosis" in Chapter VII, Section IV.)

When twenty-five or more slides of unselected village children *under* 10 *years of age* are taken and examined in the above manner the percentage in which malaria parasites are found is termed the ENDEMIC INDEX of the community.

In addition to working out this figure it is always advisable to take blood films of older children and of adults so that the observer may know the parasite rate at different ages and especially at ages above 20 or 25. The reason for this has already been mentioned on p. 15 (Chapter II).

The so-called *thick blood film method* for quick malaria diagnosis will be described later, under the heading "Diagnosis," (p. 172) but it is not applicable to field work of the above kind, because the drops of blood take too long to dry, and are usually grossly contaminated with animal and vegetable organisms from the children's unsterilized fingers and from the dust-laden air.

In addition to estimating the prevalence of malaria among the indigenous population by these methods of sampling to ascertain the spleen rate and parasite rate, an endeavour should be made to ascertain the amount and severity of "incidental malaria" among the immigrant population, and the percentage of infection in anopheline mosquitoes (*the sporozoite rate*) as described on p. 32 of Chapter III.

AN EXAMPLE OF A MALARIA SURVEY IN THE TROPICS.

I have always believed that more could be learned from a careful study of a specific example than from general directions. For this reason I have decided to introduce here the following account of an actual survey carried out some years ago in a tropical locality. The account illustrates the importance of some social and economic factors in the endemiology of the disease, and a point which has already been mentioned, namely, that in malaria surveys in the Tropics it is useful to endeavour to view the problem in a less restricted manner than the term "malaria survey" might be thought to indicate.

Object of the Inquiry.—The investigation was carried out with the object of devising measures for reducing the danger of malaria at the port of T——, which is the terminus on a large island of a new railway for traffic to an adjacent continent.

To prepare a satisfactory scheme for that object it was necessary to ascertain the circumstances and conditions of health and disease in the district generally, as well as to study in particular the special problem of malaria at the railway terminus and port. In the following account, for the sake of brevity, the information collected on both subjects is recorded together.

General Description of the District.—The names and positions of the places surveyed were recorded on a map which it is not necessary to reproduce here. They lie along, or in close proximity to, the terminal section of the railway, and in a district which, according to the Census Review for 1911, has always had the reputation of being one of the most malarious on the island. The locality is in general not more than twelve feet above mean sea-level, and may be described as being for the most part a low-lying sandy waste, upon which there are patches of scrub jungle, palmyra groves and a few coconut plantations; and almost throughout the area the subsoil water is so near the surface that, despite the porous nature of the ground, extensive tracts become flooded at the onset of the rainy season and remain so for several months.

Rainfall.—The yearly rainfall averages about 37 inches, and, as a rule, the months of the south-west monsoon are dry, and those of the north-east monsoon wet, about 65 to 70 per cent. or more of the total annual rainfall occurring from October to January. But it is important that in both amount and distribution the rainfall varies considerably from year to year; in 1902, for example, the recorded fall was as many as 55 inches, while in 1904 it was as few as 22 inches; in 1911 there was severe drought from February to October, but a severe storm causing heavy floods in December; in 1912 there was rainfall in every month except July, an unusual feature being a fall of 4·19 inches in June.

The Effect on the Population.—It is usually the case in the Tropics that abnormal meteorological conditions of any kind are adverse to the well-being of the population. and this is illustrated in the district under inquiry by the fact that years of deficient rainfall are years of scarcity and hardship, while years of excessive rainfall are years of much sickness and mortality.

Temperature.—The mean annual shade temperature of the locality is nearly 83° F., and temperatures above 100° are sometimes recorded, but during a considerable part of the year the heat is rendered less trying by strong sea breezes.

The Population and their Mode of Life.—The population consists mostly of Tamils and Moors, who are engaged in agriculture and fishing. The great majority of the people are very poor, and their standard of living is exceedingly low. Their huts are constructed from palmyra leaves (see fig. 61 below) and almost their only kind of food is provided by the young shoots of that tree. Water is obtained in the wet season from tanks and hollows, and in the dry season from primitive "wells" or water-holes dug down to the subsoil water, the sides of the hole being sometimes kept from falling in by inserting a cask, or a hollow trunk of a palmyra tree. Except in one or two of the larger villages the people have not been educated up to the need for sanitary effort, and fæcal pollution of the soil in the immediate vicinity of the houses is the rule.

Vital Statistics.—The adverse conditions with which the inhabitants of the district have to contend are reflected in the vital statistics of which the following are examples.

(*a*) In the district as a whole the following statement gives the chief rates during recent years:—

	1909	1910	1911	1912
Birth-rate per thousand	43·1	38·2	37·5	24·8
Death-rate per thousand	36·9	35·0	37·0	49·5
Infantile mortality rate	—	—	299·0	422·0

The rapidly falling birth-rate and the high rates of infantile mortality are disquieting indications from this statement.

(*b*) For the particular division with which we are chiefly concerned in this inquiry, the birth-rate works out in 1912 to 26·1 per thousand of population and the death-rate to 57·8 per thousand. The separate figures for different villages in 1912 indicate a condition which cannot fail to be a cause of grave anxiety; in some villages the birth-rate was only between 10 and 17 per thousand and the death-rate was between 44 and 77.

FIG. 61.—A line of huts constructed from palmyra leaves.

(*c*) The monthly distribution of births and deaths in the district indicate the healthy and unhealthy seasons of the year and give an idea of the causes of any fluctuations which occur at particular seasons. The analysis shows that as regards births there are two clearly marked periods, namely, from January to May when the rate is uniformly high, and from June to December when the rate fluctuates considerably, but is usually low. It is unfortunate that most births occur in the most unhealthy period of the year. The death-rate figures are also distinctly separable into two periods, namely, from January to May, when the rates are exceedingly high, and from June to December when they are comparatively low. It is clear that the great rise in mortality during the first period must be due to the annual recurrence of a fatal disease in epidemic form. It is noteworthy that the death-rate is higher than the birth-rate in every month except June, August, October and November.

Chief Causes of Sickness and Mortality.—From the statistics of the Government hospital and the dispensaries in the district it is clear that malaria is by far the most prevalent and most serious disease. Between 50 and 60 per cent. of all the cases of sickness treated at the Government dispensaries are diagnosed as that disease, or as "malarial cachexia," and it appears very probable that it is the primary cause also of a large proportion of the cases of sickness diagnosed under such headings as "fever," debility, dropsy, undefined diarrhœa, convulsions of infants, &c. Malaria also occupies a remarkable and unusual position among the chief causes of death, for of the 108 deaths that occurred in the Government hospital between 1908 and 1912, no fewer than thirty-three were ascribed directly to malaria or malarial cachexia, as compared with twenty-five which were ascribed to dysentery and twenty to pneumonia.

The marginal chart (fig. 62), which compares the seasonal incidence of the total mortality in the district with the seasonal incidence of malaria, is also of great interest in this connection, because it shows that the epidemic rise in the total mortality from January to May is due chiefly, if not entirely, to this disease.[1]

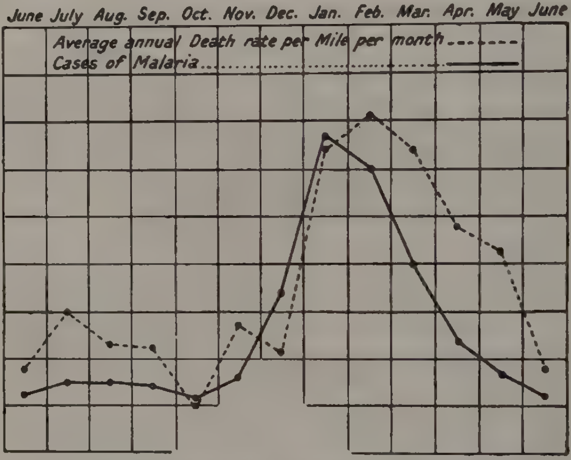

FIG. 62.—Showing the influence of malaria on the total mortality rate.

The other principal causes of sickness and death in the district are respiratory diseases, including pneumonia, and bowel complaints, including dysentery and diarrhœa; but in comparison with malaria the frequency of those diseases is not great.

Proof that the Deaths are not due to Kala-azar.—In a district where quite a considerable proportion of the deaths are ascribed to malarial cachexia there is always the possibility that some of the deaths may be due, not to that disease, but to the fatal disease called *kala-azar*, the symptoms of which have often been mistaken for those of malarial cachexia. In order to ascertain whether this was happening in the district, we selected five adult patients whose spleens were enlarged beyond the level of the umbilicus, and, after placing them in the hospital, examined specimens of blood obtained by splenic puncture. The parasite of kala-azar was not present in any of the films and this and other evidence obtained justified the conclusion that their illnesses were correctly diagnosed as malarial cachexia.

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[1] The effect of epidemic and endemic malaria on the birth-rate and death-rate in communities is usefully illustrated by Major W. H. Kenrick in a paper published in *Paludism*, No. 3, July, 1911, p. 24.

The Amount and Kind of Malaria.—Taking four villages as representative of the locality the children available were examined by the methods already described with the following results:—

(*a*) Of 167 children examined ninety-seven were found to have enlarged spleens: the spleen rate per cent. was therefore 58.

(*b*) Of 117 children from whom blood films were taken forty-two were found to have parasites in their blood: the parasite rate per cent. was therefore 36.

(*c*) Of the parasites found 71 per cent. were quartan, 18 per cent. were benign tertian and 10 per cent. were malignant tertian.

Observations on these Figures.—A spleen rate of 58 and a parasite rate of 36 were lower than might be expected, but it must be taken into consideration, first, that the parasite rate is much lower than the spleen rate; second, that the dominant type of infection found was quartan. These findings indicate that at the time of inquiry (the beginning of April) the season of new infections was almost over, for in the first place the great preponderance of quartan parasites was probably due to the fact that the number of all the kinds of parasites in the blood of the children was diminishing rapidly, but the quartan parasites, being the most persistent, were still present in sufficient numbers to be found at routine examination; and in the second place the spleen rate was still high because diminution of the size of spleens is an event subsequent to diminution in the number of parasites and is a slower process. Confirmation of the view that the season of new infections was nearly over will be seen in the chart on the preceding page (fig. 62) which shows that by April the descending epidemic curve had reached a low level. For these reasons it is probable that the splenic index of fifty-eight and the endemic index of thirty-six do not by any means represent the maximum rates for the locality.

Inference as to the amount of Malaria and its Effects.—From the foregoing account it is clear that malaria is very prevalent in the locality generally, and there seems no reason to doubt that it is the primary cause of the high death-rates, the low birth-rates, the absence of a natural increase of the population, the avoidance of the area by all who are in a position to do so, and the general backwardness of the district and lack of private enterprise in it.

Endemiology and Epidemiology.—For the reasons just given it would seem that the first need of the district is a detailed study of the endemiology and epidemiology of malaria in it with a view to ascertain the relative importance of the various factors concerned in bringing about so serious a condition, and in the hope that it might be possible by such a study to find a clue to the correct method of reducing or combating the disease. On account of the varied conditions of the different seasons such a study would require to be carried on more or less continuously for at least a year.

The few observations in connection with this study which were made during the present survey are stated under the following headings:—

THE ANOPHELES FACTOR.

(*a*) *The Kinds of Anopheles Present and their Abundance.*—Anopheles mosquitoes are doubtless very prevalent throughout the district during, and for some time after, the rainy season; but at the time of the present inquiry in April they were quite rare. Larvæ or adults of the following species were collected: *A. culicifacies, A. listoni, A. rossii, A. fuliginosus, A. jamesii, A. sinensis, A. barbirostris.*

At the time of the inquiry most of the places which would be extensive breeding grounds during the rainy season were dry. Adult anophelines were quite scarce and difficult to find, and it was only by adopting an unusual plan that we were able to secure a sufficient number to make it worth while going to the labour of dissecting them for the detection of zygotes and sporozoits. Larvæ of *culicifacies* were collected from borrow pits and from the primitive water-holes which serve the inhabitants as wells. The only specimen of *listoni* obtained was bred from a larva collected in a natural pool. Specimens of *fuliginosus* and *jamesii* were bred from larvæ collected in a weed-grown natural pond in the compound of one of the European's bungalows. This was also a breeding place of *sinensis* and *barbirostris*, and of four species of culicine mosquitoes. Large numbers of the larvæ of *rossii* were collected from the extensive sheet of water shown in the following photograph (fig. 63).

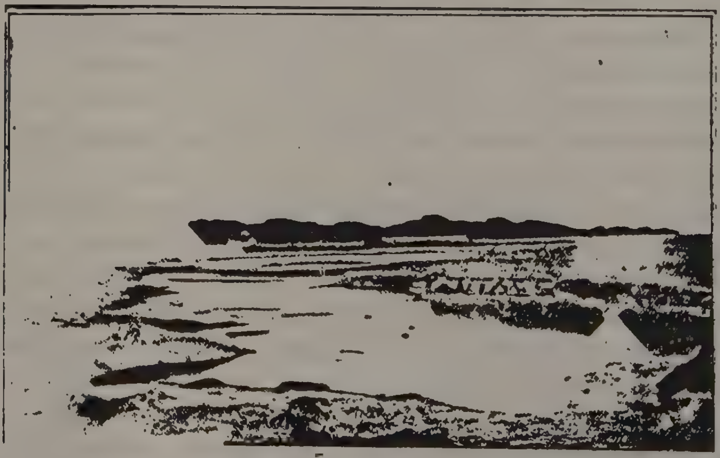

Fig. 63.—An extensive breeding-place of *Anopheles rossii.*

(*b*) *The Carrier of Malaria in the Locality.*—By usual methods of search in houses in the early morning we were unable to catch any adult anophelines for purposes of dissection. Dr. S. T. Gunasekara, who accompanied me on the inquiry, therefore volunteered to adopt a plan which I had found successful in other localities. With two assistants, who were good mosquito-catchers, he sat up for several nights in an occupied hut which was lighted just sufficiently to enable any mosquito which might settle on his bare wrist or hand to be seen and caught in a test-tube. He and his assistants were bitten several times during this work, but they succeeded in catching about forty adult female *culicifacies.* I dissected thirty-six of these and found sporozoits in the salivary glands of one specimen. For this reason, as well as because it was the only species which could be collected in houses, it was probable that *A. culicifacies* was the chief malaria-carrying species at the time of our inquiry.

THE FACTOR OF THE SOCIAL AND ECONOMIC CONDITION OF THE PEOPLE.

On p. 15 (Chapter II) it was noted that—as was originally pointed out by Stephens and Christophers in India—the lower the social status of the people (or, in other words, the more severe the conditions of life) the greater will be the amount and severity of malaria. In the villages included in the present survey the inhabitants are poverty-stricken and live in a condition of general squalor associated with much privation and hardship. It is not surprising that in such circumstances the effects of malaria should be more severe, and infection once contracted should persist for a longer time, than among people who are well housed and well fed. Of all the villages which we visited K— seemed to be the one in which the people were poorest, and their manner of living most hard; and in this village, although at the time of inquiry we found no anophelines and no facilities for their breeding, the splenic index was 100 as compared, for example, with an index of only 34 in P—, in which most of the people seemed to be fairly prosperous but in which anophelines were found and the facilities for their breeding were not rare.

THE FACTOR OF RESIDUAL INFECTION.

Christophers and Bentley have pointed out that the way in which the economic conditions just mentioned influence malaria is by favouring relapses and a state of continuous infection (residual infection). The result is that a very few anophelines suffice to maintain a high degree of parasite infestation. The community under inquiry is one in which, during periods of scarcity and unusual meteorological conditions, the amount of sickness and mortality from malaria increases independently of an increase in the number of anopheline mosquitoes.

THE FACTOR OF NON-IMMUNE IMMIGRATION.

One of the characteristics of malaria in the district is that in villages where the population is fixed and permanent the disease is chiefly confined to the children.

For example, in the village of K— the spleen rate among the children was 100 per cent. and the parasite rate 50 per cent., while among the adults these rates were only 15 and 8 respectively. The adults are not less exposed to infection than the children, and the explanation of the lower rates among them is that they have become more or less immune by repeated and long continued infections (see p. 15, figs. 10 and 11). It always happens that the introduction of non-immune immigrants into villages of this kind leads to a sudden burst of increased malarial infection in which the new-comers are chiefly involved (*incidental malaria*). When the number of non-immune immigrants is sufficiently great, the result is the production of an epidemic which affects all classes of the community; and such an epidemic may arise even at a time when the number of anophelines in the area is small—the epidemic being one in which the "human factor" rather than "the anopheline factor" is the chief influence at work. Conditions of this kind make the problems connected with the employment of outside labour in the district difficult, prevent colonization, and hinder progress generally.

In this connection it is appropriate to introduce here the observations made on the prevalence of malaria among the temporary labour force which was engaged in constructing the railway and buildings at the port. A Government report states that during the first year of the railway work the area acquired an evil reputation, and it appears from the statistics available that from the commencement of the work malaria was rife among the labour force. The figures of the Government dispensaries show that every coolie employed must have been ill several times during each year, and the records of the labour rolls indicate (according to an examination made at the time of our visit) that on an average an ordinary unskilled coolie apparently puts in only about eighteen working days per month. In 1910 the death-rate among the native labour force employed at the port was forty-six per thousand of the average daily strength. The following results of personal examinations of adult working coolies were obtained during the inquiry:—

(*a*) Of forty-one adult coolies examined by random sampling eleven were found to have enlarged spleens and fourteen were found to have malaria parasites in their blood. These figures give an adult spleen rate of 27 and an adult parasite rate of 34.

(*b*) Of 156 other coolies examined the rate of splenic enlargement was found to be 20 per cent.

(*c*) Of ninety coolies who were asked as to the condition of their health no fewer than seventy complained of having had fever recently.

(*d*) Among working coolies we found five examples of true malarial cachexia and a number of cases in which severe malarial anæmia was present.

(*e*) Of thirty-four coolies from whom we inquired the length of their residence on the work, sixteen had arrived less than three months previously. The parasite rate among these new arrivals was 44 per cent., while it was only 20 per cent. among those who had been resident a year or more.

(*f*) Among the coolies examined there was one man who had been on the work for three and a half years, who appeared healthy and strong, who assured us that he had suffered from fever only once (shortly after his arrival) but whose blood might almost be described as being "swarming" with malaria parasites. A "chronic parasite carrier" of this kind, upon whom the parasite has ceased to exercise any very obvious effect, is a great infector of anophelines and a serious danger to the health of the community.

THE ANNUAL EPIDEMIC AND THE FACTOR OF RAINFALL.

It has already been noted that in the district generally there occurs, in addition to, and superimposed upon, the endemic form of malaria which persists throughout the year, an annually recurring epidemic beginning as a rule at the end of November and lasting until April. The following chart shows the relation of this epidemic to the rainfall.

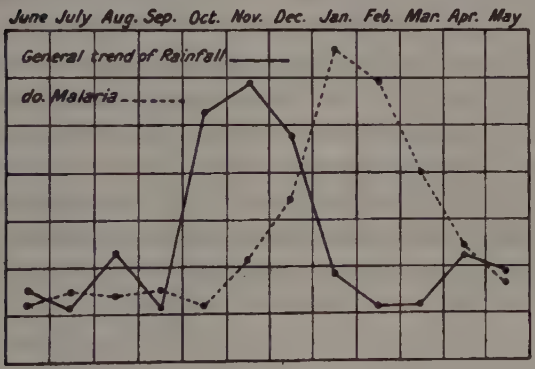

Fig. 64.

It will be seen that the epidemic begins about six weeks after the onset of a rainy season which causes extensive tracts of the country to be in flood. The period of time is sufficient for a great increase in the abundance of anophelines and for a great number of them to become infected, and this may well be the manner in which the rains act to bring about the epidemic. But it is really of less importance to know the exact manner in which the rains act than it is to realize that the floods which they produce are the prime factor in the production of the epidemic, and that as regards the district generally, measures which did not prevent these floods or their effects would hardly be likely to yield any permanently good result.

FACTORS OF GENERAL AND PERSONAL HYGIENE AND WELL-BEING.

The inquiries under this heading had reference to the knowledge that in malarious places the absence of special precautions to ensure the physical comfort and well-being of labourers is usually followed by a condition of physiological poverty, which is very favourable to an increased prevalence and severity of malaria. It is not necessary to give the results of the inquiries in the particular survey now being described, but it may be useful to note that they were concerned with the arrangements for ensuring that the labourers could obtain an adequate dietary proportional to the amount of work expected of them; that they were suitably housed; that they had an abundant supply of pure water; that they had a sufficient supply of fuel and other materials for cooking their food; that they had the means and facilities for indulging in the small luxuries such as tobacco, &c., to which they are accustomed in their own homes; and that there were suitable and accessible arrangements for their treatment when ill. In connection with inquiries into wages and the prices of foodstuffs it must be remembered that a labourer's daily wage may be favourably high, but that if he is prevented by illness from working more than eighteen days in a month, his total monthly earnings may not be more than sufficient to provide him with bare necessaries.

THE PLAN OF ACTION RECOMMENDED.

The above account gives the chief observations which were made in the particular survey described, but the survey would be incomplete without an endeavour to formulate from these observations "a precise plan of action which, with a knowledge of the financial and other circumstances of the locality, will be a plan which it is practicable to carry out" (p. 81, Chapter V). That is an essential part of the survey, but the present example is more complete than the example which was given in Chapter V and cannot be suitably dealt with until we have described the general principles on which anti-malarial action in the tropics is based. I propose therefore to defer its consideration to the chapter on the prevention and eradication of malaria, in which it will be convenient to be able to refer to the results of this survey when illustrating certain points.

CHAPTER VII.

The Symptomatology, Pathology and Diagnosis of Malaria.

IT is well known that the great majority of cases of illness due to infection with malaria parasites present a striking clinical picture in which FEVER, ANÆMIA and SPLENIC ENLARGEMENT are dominating and almost constant features. As a rule the only other conspicuous symptoms and signs are referable to the digestive and nervous systems. In these typical cases the characteristic symptomatology comprises a primary series of paroxysms of fever and anæmia, followed, after a variable period of apyrexia and apparent recovery, by a number of secondary series of similar attacks which are called relapses. At first these relapses tend to recur at intervals varying from a week or ten days to a fortnight or three weeks; later (in the absence of reinfection) they become less frequent, so that several months, or even a year, may pass without an attack. Each febrile attack, if recognized at a sufficiently early stage, always yields to proper treatment by quinine; but up to the present there is no known drug which will effect a permanent cure. For this reason malaria is a disease which always lasts a long time and causes much ill-health and disability.

At the outset of our clinical study it should be noted that in malarious countries there is a great difference between the symptomatology during years or circumstances of normal endemic incidence and during years or circumstances of exceptional epidemic prevalence. The illness which arises during ordinary years, whether it is due to the so-called "benign" forms of the parasite (*P. vivax* and *P. malariæ*) or to the so-called "malignant" form (*P. falciparum*) is comparatively mild and is only rarely followed by a fatal issue: the illness contracted during epidemic years or conditions is always serious and is directly responsible for a large number of deaths even among persons who have acquired a considerable degree of tolerance to the usual endemic infection. The war has afforded many opportunities of studying the serious manifestations of malaria which occur in times and circumstances of great epidemic intensity, but it should be remembered that, while taking due note of the clinical picture which writers with war experience only have recently presented, it would be quite wrong to regard this as illustrating the type of disease which will be commonly met with in practice during peace-time in the Tropics. This type will most frequently be one in which the physician's chief endeavour will be to convince the patient that it is necessary to treat seriously an illness which incapacitates him for only a few days each month, and which he has learnt to regard, if not with contempt, at any rate with equanimity, "because it does not kill." [1]

Having in view the great variety of clinical types which come between the dangerous epidemic form of the disease on the one hand and the relatively innocuous endemic form on the other, no one who sets out to provide a simple, yet sufficiently complete, account of the symptomatology of malaria can fail to be apprehensive of the magnitude of his task and of the difficulty of arranging the matter at his disposal in a way that will be profitable to students who are approaching the subject for the first time.

I have decided to attempt the task in four sections as follows :—

Section I.—A connected clinical account, in broad outline, of the onset, course and termination in uncomplicated cases which form the great bulk of the cases met with in practice.

Section II.—Further clinical details and a pathological statement of each of the symptoms (fever, anæmia, splenic enlargement, &c.) which are commonly or rarely observed in different cases of malaria.

Section III.—(1) On deaths from malaria; (2) On malaria in children; (3) On pernicious symptoms; (4) On other complications and sequelæ.

Section IV.—The diagnosis of the disease.

SECTION I.

A CLINICAL ACCOUNT OF THE ONSET, COURSE, AND TERMINATION IN ORDINARY CASES.

The Incubation Period: Latent Infections.—The time which elapses between the date of being bitten by an infected mosquito and the date when the earliest clinical symptoms are felt by the patient varies with the dose of sporozoites injected, the virulence of the particular strain of parasite, and with the different factors which tend to lessen or to increase the patient's resisting power. The usual incubation periods in naturally acquired infections are, in malignant tertian malaria, nine to twelve days; in benign tertian malaria, fourteen to eighteen days; and in quartan malaria, eighteen to twenty-one days; but the period may be shorter or longer, and as regards the maximum period it is the case that in some persons, whose infection has been with only a small number of sporozoites, no symptoms appear and no parasites can be detected in the peripheral blood until several months, or even a year, after the infection was contracted. Recently a number of instances of this nature have come to notice in England in regard both to soldiers who must have contracted their infection in Salonika and in regard to children who must have become infected in this country. They are correctly described as being instances in which the infection has remained "latent." The following are examples :—

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[1] In a malarious locality in Assam during an investigation into the very serious disease named *kala-azar*, a native woman who was suffering from fever, anæmia, and enlarged spleen, was asked why she did not go to hospital for treatment. She replied: "If I have got malarial fever I shall get well sooner or later anyhow, but if I have got *kala-azar* nothing can cure me, so what is the use of bothering me with medicine?" Many Europeans regard malaria from the same point of view.

(1) E. J. S., aged 35, of Wood Green, London, was demobilized in February 1919. He had served in the Army two years, of which three months had been spent in Salonika and the remainder in Egypt and Palestine. He is a well educated business man whose considered statement that he "had never had a day's illness during the whole of his service," can be accepted without question. After being demobilized he resumed his usual occupation as a commercial traveller in England. He carried on this work for four months "without an hour's feeling of seediness" until, in the third week of July, 1919, he had an unexpected feverish attack which at first was thought to be influenza. A day or two later the character of the symptoms suggested the possibility that the attack might be malarial in nature and a blood film sent for examination was found to contain many benign tertian malaria parasites. The result of a local investigation negatived the view of an infection contracted in this country and it was therefore decided to class the case as an example of "long latency."

(2) In March, 1918, Mrs. H., who had never been out of England, and whose home is in a crowded London district where there are no anopheline mosquitoes, was taken ill with a typical attack of malarial fever, benign tertian parasites being found in her blood. She stated that she had not suffered from an illness of any kind for at least a year, and had never previously had an illness of this character. On inquiry it was ascertained that she could not have contracted the infection in her home in London, but that in September of the previous year she had stayed a few days in the Isle of Grain in a mosquito-infected house where several cases of indigenous malaria had occurred. For this reason it seemed clear that Mrs. H. had contracted her infection during that visit and that the infection had remained latent until the spring of the following year.

In a good many cases of latent infection the primary attack is delayed until the person is subjected to unusual physical or mental stress,[1] or privation, or exposure or other condition which tends to lower his resisting power. For this reason it has happened frequently that regiments which have been comparatively free from malaria while carrying on their usual routine peace-time duties have shown an "epidemic incidence" shortly after commencing forced marches or other arduous duties in the field.

The term "latent infection," as used above, signifies an infection in which for some time beyond the usual incubation period of the disease the results of the infection are not apparent either by the onset of symptoms *or by blood examination.* In primary infections it often happens that symptoms appear before parasites can be detected in the peripheral blood, but the condition in which parasites can be found before the appearance of symptoms, although common enough in chronic cases, has not occurred in my experience of the primary disease. (See also the remarks under Diagnosis p. 171).

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[1] Surgical operations are frequently an exciting factor. See an article by Dr. M. White in the *Lancet* of July 26, 1919, p. 154.

Mild Ambulatory Cases.—Closely allied to cases in which the infection remains latent for a long time are certain cases in which the symptoms caused by a definite infection are so slight as to be hardly noticed by the patient. A number of mild ambulatory cases of this kind occurred during the war in soldiers who were taking prophylactic doses of quinine, but the condition has also been observed in cases in which no quinine was being taken. Several of the indigenous cases of malaria which have recently occurred in England have been so mild that the patient has complained of little more than "occasional cold shivers"; and even in malarious places in the tropics the primary illness in many cases incapacitates the patient for only a few hours, or a day or two, and is soon forgotten. A patient seen in such an attack usually complains of "being out of sorts" with headache, chilliness, stiffness of the neck or aching in the back, and perhaps unusual sweating. The temperature may be found to be about 99° or 100° F., but in an hour or two it declines rapidly to normal or below. Parasites can seldom or never be detected in the peripheral blood in mild primary attacks of this kind, but, if no quinine is given, the patients often suffer on a subsequent occasion from a definite relapse in which parasites can be easily found.

It is important to make a distinction between the classes of case just described (namely, those in which the primary infection remains latent or causes symptoms which are of only a mild ambulatory type) and the class of case in which a person who has suffered from repeated attacks does not feel any symptoms because he has acquired a tolerance to the effects of the parasitic invasion. In the latter class of case the infection has not remained latent; parasites can easily be found in the peripheral blood, and inquiry will show that during the primary attack and subsequent relapses the patients had suffered severely. The correct description of a case of this kind is that the person is an "apparently healthy malaria-parasite-carrier." Such persons are on the way to become immune to infection, but persons in whom an infection has remained latent possess no immunity and are liable at any time to suffer from a severe attack.

The Onset in other Atypical Cases.—From what has just been said it will be clear that the primary illness does not always commence with very characteristic symptoms and signs. Indeed an atypical onset has been observed so frequently in primary cases of malaria contracted during the War that it is advisable to keep in mind the possibility of malaria as regards almost every illness in which, after proper clinical examination, some doubt as to the diagnosis remains. And in view of the frequency with which persons who have served in the War have not suffered from their first attack of malaria until after their return home, this is true for cases of illness occurring in temperate as well as in tropical countries.

The following examples are briefly recorded in preference to giving a general description of the onset in some atypical cases.

(1) J. I., aged 23, joined the Army in July, 1915, and after serving at home and abroad, was demobilized from Brussels in February, 1919. Soon after entering the Army he suffered severely from influenza, and in August, 1917, he was wounded. No history of any other illness or disability during his Army service could be elicited, and he stated that he was sure he had never suffered from malaria, "or anything like it." On his return to England early in 1919 he resumed his civil occupation in London as a tailor. He was quite well until the end of May, when he began to suffer from loss of appetite, dyspepsia and "general weakness." The symptoms were attributed to the change from an open-air life to a life in an East End tailor's shop, and little notice was taken of them. But it worried him that he was getting pale and losing flesh, that his mind did not seem clear, that he felt weak and tired, and that his "dyspepsia" sometimes caused vomiting. Early in July he sought medical advice, and his illness was diagnosed as gastric influenza, for which he was treated during the next two or three weeks. Towards the end of the month a suspicion of malaria arose from the observation that the attacks of vomiting were at intervals of two days. A blood film was then sent for examination and was found to contain a considerable number of benign tertian malaria parasites.

(2) On July 21, 1919, R. B., aged 7 years, was taken by his mother to the Essex County Hospital, Colchester, "because he had bled a lot from the mouth and nose." The mother said she had noticed lately that he had been getting very pale but that otherwise he seemed quite well. He was admitted to hospital. The notes made on admission record the following points: "The child is very pallid, but otherwise seems fairly well; the heart and lungs are normal but the liver and spleen are greatly enlarged, as shown in the accompanying diagram (fig. 65); there are no other abnormal signs in the abdomen and there are no enlarged glands; no sponginess of the gums."

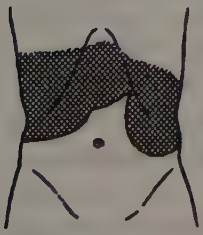
FIG. 65.

At the time of admission (10 a.m.) the temperature was 98° F., but at 2 o'clock it was found to be 104·6° F. It fell as rapidly as it had risen and was normal at 8 p.m. "The fever was not accompanied by any rigor or shivering and there was no special sweating. The patient made no complaint of illness." On the next day a blood examination was made with the following results; *Red cells* 2,200,000; *Hæmoglobin* 47 per cent.; *Leucocytes* 4,490; *Differential count of leucocytes:* polymorphonuclear 34·6 per cent., lymphocytes 60·1 per cent., transitional cells 5·1 per cent., eosinophil cells 0. *Examination for parasites*—"Films stained with Leishman's stain showed a considerable number of benign tertian malaria parasites, two groups being present (double tertian)."

The patient was then put on quinine sulphate, 3 grains three times a day. The temperature after admission is shown below (fig. 66).

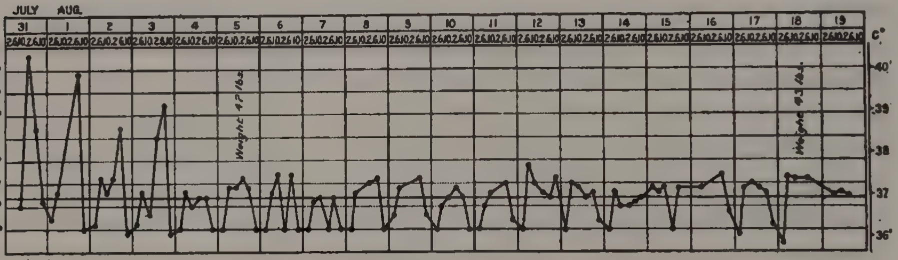

FIG. 66.—Chart of R. B.

(3) On October 12, 1919, A. C., aged 15, was admitted to the Victoria Hospital, Southend-on-Sea, suffering from remittent fever which was thought to be due to a septic condition of the mouth. The temperature chart after admission is reproduced below (fig. 67).

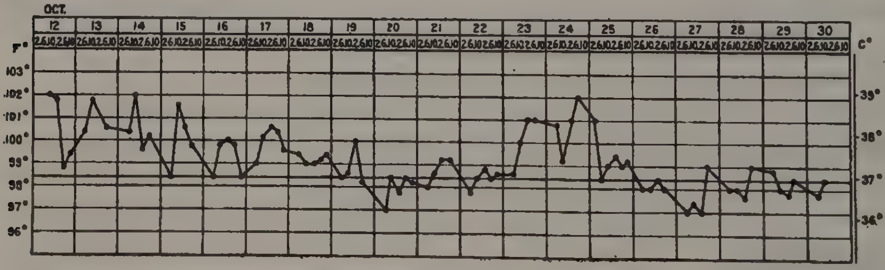

FIG. 67.—Chart of A. C.

Blood examination showed that the patient was suffering from benign tertian malaria. The infection had been contracted in England.

The Onset in Typical Cases.—Typical primary cases are considered to be those in which, after perhaps one or two days of somewhat indefinite illness, the occurrence of definite attacks of "ague" at regular intervals leaves no room for doubt as to the diagnosis of the disease. The great majority of new cases of malaria are of this type, which is illustrated in the following examples of experimental infection.

(1) An Indian hospital assistant, who was sceptical as to the mode in which malaria is contracted, permitted some infected mosquitoes to bite him from the 21st to the 25th of January. He remained well until the 3rd of February, which was the thirteenth day after he was first bitten. On that day he felt "seedy" and "out of sorts" and his temperature was found to be 99° F. One parasite was found in a blood film after long search. Next day he felt well again but on the third day he had a typical shivering fit with a rise of temperature to 104° F. Parasites were readily found in his blood. He allowed the illness to run its course for five days during which he had two more typical attacks with the cold, hot and sweating stages well marked. Being by this time quite convinced of the truth that mosquitoes convey the disease he stopped the recurrence of further attacks by taking quinine.

(2) Between the 29th of August and the 4th of September, 1900, Sir Patrick Manson's son, the late Dr. P. Thurburn Manson, who was at that time in England, permitted himself to be bitten by ten anophelines which had been infected from a patient in Italy who had two groups of benign tertian malaria parasites in his blood. Dr. Manson described the onset of the subsequent illness as follows:—

"Up till September 13th I had been perfectly well. On the morning of that day I rose feeling languid and out of sorts with a temperature of 99° F. By midday I was feeling chilly and inclined to yawn. At 4·30 p.m. I went to bed with severe headache, sensation of chilliness, lassitude, pains in the back and bones, and a temperature of 101·4° F.

"September 14th: I slept fairly well, but woke at 3 a.m. with slight sweating and a temperature of 101° F. During the day my temperature ranged between 101° and 102° F. The symptoms of yesterday were exaggerated and anorexia was complete.

"September 15th: Woke at 7 a.m. feeling distinctly better, but with a temperature of 100·4° F. About 2 p.m. I commenced to feel slightly chilly: this soon wore off and I became hot and restless. By 4·30 p.m. the temperature was 103·6° F. It remained about 103° F. till 9 p.m., when profuse sweating set in. I am told there was some delirium.

"September 16th: I woke at 8 a.m. feeling quite well; temperature 98·4° F. In the afternoon and evening there was a recurrence of fever (temperature 102·8° F.) relieved by sweating.

"September 17th: Again felt quite well on waking after a good night's sleep; temperature 99° F. About 2 p.m. the sensation of chilliness returned. By 5 p.m. the temperature had reached 103° F. Then there was copious sweating. The edge of the spleen could be felt on deep inspiration and there was a slight feeling of discomfort in the region of that organ. By 9 p.m. the temperature had fallen to 99·2° F. and I was feeling better. Quinine was given.

"September 18th: Woke after a good night feeling perfectly well (temperature 97° F.)."

In this case malaria parasites were not found by blood examination until the 16th September, which was the fourth day of illness, and they became numerous on the fifth day. The administration of quinine cut short the illness and caused the parasites to disappear from the blood.

The Developed Disease in Primary Cases.—In a primary untreated attack of uncomplicated benign tertian or quartan malaria, even when the onset has been atypical, not many days elapse before the illness assumes a definite type characterized by the recurrence of paroxysms of fever at regular intervals which may be every day, or every two days or every three days. Especially in the true intermittent fevers caused by *P. vivax* and *P. malariæ* each febrile paroxysm is accompanied by characteristic symptoms represented clinically by a "cold" stage, a "hot" stage and a "sweating" stage. At the beginning of the cold stage the patient feels chilly; he shivers and becomes very pale and ill-looking. Quite quickly the sensation of cold spreads all over his body and becomes so intense that his teeth chatter and he shakes from head to foot. Vomiting is frequent at this stage. He crawls to bed, covers himself with all the blankets and rugs available, and curls himself up so as to present as small a surface as possible. The lips and nails are livid, the skin appears bloodless, and the extremities very cold. It is often difficult to feel the small rapid pulse and, on account of his shaking condition, the patient takes only shallow quick breaths with difficulty.

The duration of the cold stage is very variable; perhaps in most cases it lasts two and a-half or three hours, but quite often it is over within an hour. The temperature begins to rise before the commencement of the hot stage, which usually starts with a feeling of warmth, comfort and considerable relief. Soon, however, the skin becomes dry and burning, the head throbs, the face is flushed, and the temperature rapidly rises to 103° or 104° F. or higher. Transient delirium is not uncommon during this stage and the patient throws off all the bed-clothes in the vain endeavour to get cool. Usually within one or two hours the temperature begins to fall very rapidly and the sweating stage sets in. The perspiration is usually profuse and has a peculiar sperm-like smell. During this stage the patient feels exhausted and often sleeps for an hour or two, then wakes in a bath of perspiration. Within four or five hours all the acute symptoms subside and the patient feels almost well.

We may now examine briefly some temperature curves of typical cases in this stage of the disease.

Fig. 68 represents a usual temperature curve in a case of infection with one group of benign tertian parasites.[1] In this type of malaria the temperature rises very quickly and is often higher than in either of the other forms. The duration of the paroxysm, however, is short, and the fever is seldom accompanied by serious symptoms.

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[1] *Note.*—The charts which follow have been purposely reduced to a size which enables them to be printed in the text. In some instances it may be necessary to use a reading glass to ascertain the details which are written upon them.

There is a sharp rigor, a quick onset of fever, free perspiration and a rapid fall of temperature, the whole paroxysm being completed, as a rule, within from six to ten hours. On the intervening days there is seldom any fever, and the patient is usually able to get up and carry on his occupation. This type of fever has a great tendency to relapse.

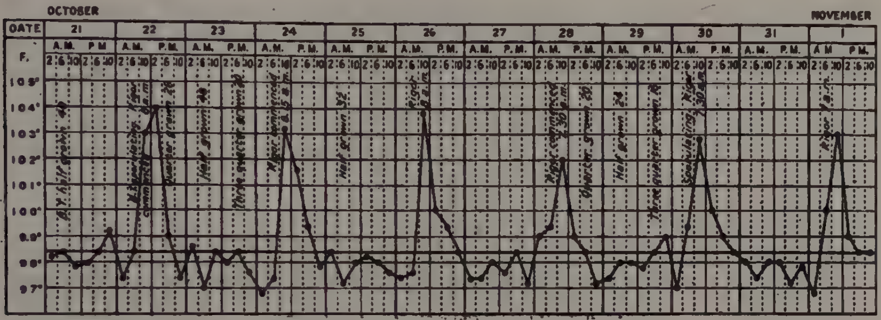

FIG. 68.—Pte. B. Infection with one group of benign tertian parasites. No quinine treatment. In examining the chart note the following points: (1) The rigors began at 8 a.m. regularly until the 28th, when they commenced "to anticipate" by about half an hour; (2) the course of the temperature can be correlated with the stages of growth of a parasite which takes forty-eight hours to complete its cycle; (3) sporulating forms were found about an hour before the rigor commenced; (4) the fever rises very suddenly but falls less suddenly; (5) B.T. 40 means that 40 parasites were found in 100 fields.

Almost as common as the pure tertian type of fever is the type due to more than one group of benign tertian parasites in which there is a paroxysm of ague every day. This "double tertian" type is caused typically when the patient's blood contains two groups of parasites which sporulate on different days, but in practice it is also the usual type in patients whose blood contains a number of groups or "broods" of benign tertian parasites in various stages of growth. Fig. 69 is the chart of a case of this kind.

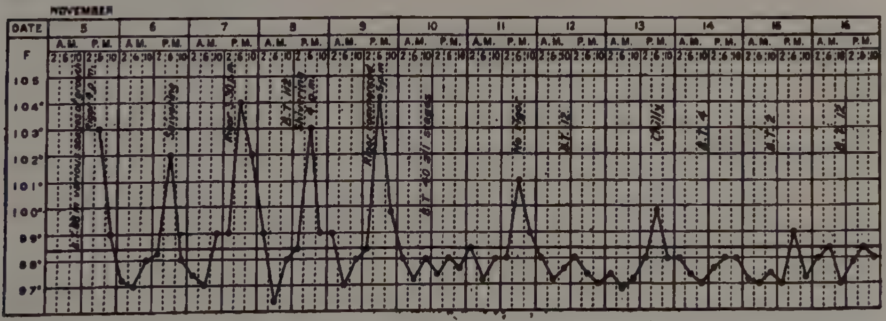

FIG. 69.—Pte. Y. Infection with various groups of benign tertian parasites. No quinine treatment. Note (1) the large number of parasites; (2) the regular daily febrile paroxysm cannot be correlated with the stages of growth of the parasites; (3) the febrile paroxysms ceased although no quinine was given; (4) the parasites did not entirely disappear from the peripheral blood.

Fig. 70 represents the classical temperature curve in a case of infection with one group of quartan parasites.

In this type of malaria the paroxysms are of comparatively short duration and the temperature seldom rises above 103° or 104° F. The paroxysms recur with greater regularity than in either of the other forms of malaria, and they persist for a longer period. It is quite common for untreated patients to have a paroxysm every fourth day for a month or six weeks. The fever-free interval of two days between each paroxysm allows time for partial recovery, and many persons who have gone through ten or fifteen paroxysms present remarkably few obvious signs of illness excepting great enlargement of the spleen. Major Andrew Buchanan's book on "The Malarial Fevers and Malarial Parasites in India" contains records

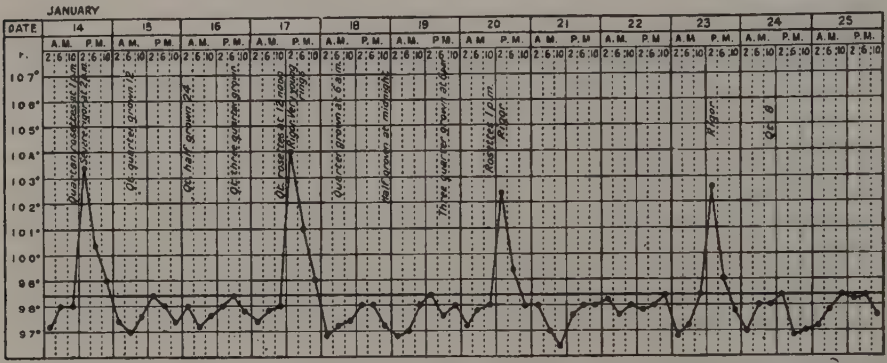

Fig. 70.—S. K. Infection with one group of quartan parasites. No quinine treatment. Commencing with the stage of very young rings at 2 p.m. on the 17th follow the growth of the parasites to the stage of rosettes at 1 p.m. on the 20th. Note the finding of rosettes about an hour before the commencement of the rigor.

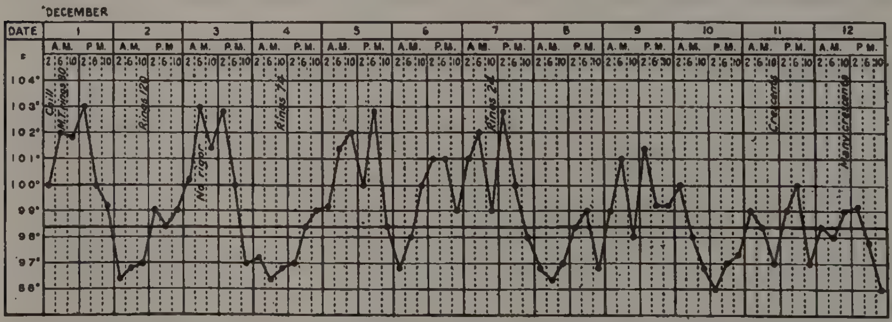

Fig. 71.—C. Typical infection with malignant tertian parasites. Note (1) rings 120 means that 120 parasites, all in the "signet ring" stage were found in 100 fields; (2) for the first few days the chart is definitely tertian in character; (3) the febrile paroxysm lasts a long time (about eighteen hours); (4) the "switchback" character of the fever, especially on the 6th and 7th; (5) the appearance of crescents on the 11th day.

of several untreated patients who actually gained in weight during long periods of regularly recurring paroxysms.

Fig. 71 represents the typical temperature curve in an infection with a single group of malignant tertian parasites. In practice regularly recurring paroxysms every other day are seldom observed in this type of fever. Commonly there is fever every day; it is usually intermittent, but may be remittent or quite irregular, and definite stages of "rigor," "heat" and "sweating" are seldom apparent. It will be seen from the chart that in this form of malaria the paroxysm of fever lasts much longer than in the benign tertian or quartan variety. The typical fever-curve described by Marchiafava and Bignami comprises initial rise, pseudocrisis, precritical elevation and true crisis. The time occupied is usually not less than from twelve to fourteen hours, and a second paroxysm often begins before the first paroxysm has ended. Severe vomiting, delirium and other cerebral symptoms are frequent in this type of malaria.

Some observers describe a type of malignant fever in which a regularly recurring daily paroxysm is said to be caused by a parasite which completes its cycle in 24 hours. Fig. 72 represents this type.

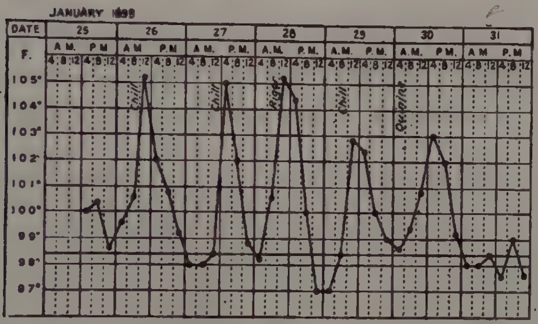

FIG. 72.—Quotidian æstivo-autumnal fever (after Craig). Some observers consider that this type of malignant fever is caused by a special variety of parasite which completes its cycle in twenty-four hours.

The general course of the illness differs in malignant tertian fever and in the true intermittent fevers due to the benign tertian and quartan parasites. In malignant tertian fever the primary attack, even when untreated, is of about a week's duration. Towards the end of that period the temperature chart shows a characteristic "downward slope." The first apyretic interval lasts only a few days, and is followed by the first relapse which is often more severe than the primary attack, but lasts about the same time. Thereafter the patient (when untreated) usually suffers from four or five relapses of declining severity at intervals of approximately ten or twelve days. Then the relapses cease for a considerable time. Afterwards they come on only at irregular intervals and in less severe form. The disease as a whole, though the symptoms are more serious than those of benign tertian and quartan fevers, is less protracted and is often more quickly cured than is the case with those types. In untreated benign tertian and quartan fevers the general course is less regular. The duration of the primary attack is very variable; sometimes it comprises only two or three definite paroxysms; sometimes there is a paroxysm every two days or every three days for as long as two months. After the primary attack the fever-free intervals between the relapses vary between ten days and three weeks. As time goes on, although the relapses tend to recur less frequently, they maintain for a year or more their original severity.

The Developed Disease in Reinfected Cases.—In malarious localities in the tropics perhaps the commonest type of case met with is one which results from repeated infections and reinfections in consecutive years. Such patients have usually acquired some tolerance to the effects of the parasitic invasion and, although the physical signs are typical, the symptoms are less typical than in the clear primary case. The following are examples:—

(1) *An Untreated Infection and Reinfection with Benign Tertian Parasites.*

H., a native of India, had an attack of malaria in October, 1901. It lasted, a month. The fever usually came on every night, "but on some nights it was not so bad as on others." He had no treatment for it. It was followed by similar but less prolonged attacks at irregular intervals and he was suffering from one of them when he was seen on April 4, 1902, which was six months after his primary attack. His spleen was enlarged nearly to the umbilicus and he was very anæmic, but his illness did not incapacitate him from work. There were many benign tertian parasites in his blood. As a result of this relapse his spleen enlarged to 1 in. beyond the level of the umbilicus. During the summer months the fever came on only in short relapses at long intervals and he improved greatly. Several examinations of his blood in June did not reveal the presence of parasites or pigment. On November 1 a few benign tertian parasites were again found (probably the result of a new infection) and systematic examinations and records of temperature were commenced on the 4th. The temperature chart for nearly three months from that date is reproduced above (fig. 73).

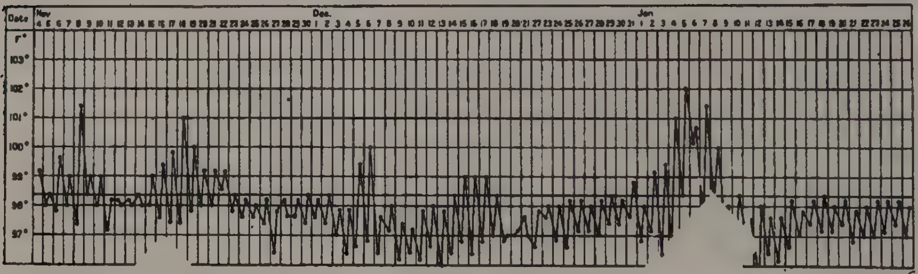

FIG. 73.—Chart of H——.

It will be seen from this chart that, during the three months, the patient had five attacks of fever, none of them being of longer duration than eight days. He received no treatment. The attacks were not severe, but while they lasted he was now and then incapacitated from work and complained of loss of appetite and occasional vomiting. The febrile paroxysms usually began with a feeling of chilliness and shivering, but "cold," "hot" and "sweating" stages were not marked. It will be noticed that on this chart, which is of temperatures taken only twice daily, the fever seldom shows any indication of the periodicity which is so characteristic of typical benign tertian infections. To observe the periodicity in cases of this kind the temperature must be taken at least every four hours, and preferably every two hours. In the present case one of my assistants, by remaining in the patient's house for several nights during the relapse of fever which began about the 31st December, was able to obtain the two-hourly chart which is reproduced in the margin (fig. 74).

This chart shows very clearly two major paroxysms at an interval of forty-eight hours and two minor paroxysms at an interval of forty-eight hours. The major paroxysms began at 8 a.m. on the 5th and at 10 a.m. on the 7th, the minor paroxysms at 12 noon on the 6th and 8th. The duration of the major paroxysm on the 5th was quite twenty-four hours, but on the 7th it was hardly eighteen hours: the minor paroxysms lasted about eight hours. Microscopic examination showed that in the blood of this patient (who had doubtless been infected and reinfected many times) there were several groups of benign tertian parasites in different stages of growth. To this was due the somewhat complex character of the temperature chart.

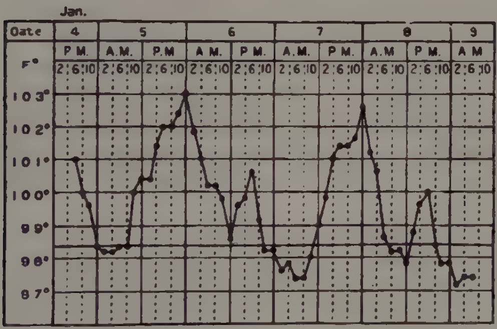

FIG. 74.—Two-hour chart of H——.

During the apyrexial intervals freedom from symptoms was almost complete and except for the splenic enlargement and anæmia it would not have been easy to diagnose the case.

(2) *An Untreated Case of Malignant Tertian Infection and Reinfection.*

B., a native of India, aged 10 years. This boy was examined for the first time on April 10, 1902. His parents said he had suffered from fever "off and on" for about five months. He was fat and cheerful, and did not appear ill; but examination showed that he was very anæmic, and his spleen was enlarged 3 in. below th costal margin. On the evening of April 10 his temperature was 101° F., and crescents and pigmented leucocytes were found in his blood. Three weeks later his spleen was about the same size, and crescents were still present. At the end of June the spleen was only 1 in. below the ribs; no parasites could be found. At the end of October he began to suffer from fever again, probably as the result of a new infection. On November 1 the spleen was found to be 2 in. below the costal margin, and a few malignant tertian rings were present in his blood. A record of the temperature for three months from this date is reproduced below (fig. 75).

The chart, as in the previous case, shows five periods of fever. Three of them lasted about twelve days and two about five days. During these relapses the child was obviously ill and suffered considerably from vomiting and diarrhœa. But during the fever-free intervals the presence of an enlarged spleen was the only obvious sign of malaria, and the child played with others in the village as if perfectly well. A two-hourly temperature chart was obtained during some days of the relapse which began on January 1 and is reproduced here (fig. 76). It will be seen that in the paroxysm of January 4 the temperature rose to 100·8° F. at 4 p.m.; it then dropped to 99° F. at 6 p.m., but rose again to 101·4° F. at 10 p.m. This "switchback" type of fever appears again on each subsequent day, and is characteristic of malignant tertian fever.

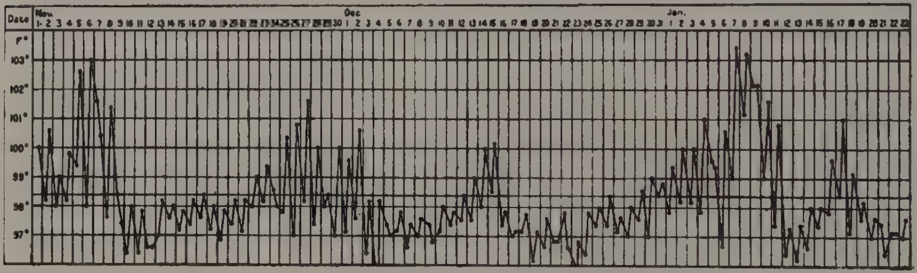

Fig. 75.—Chart of B——.

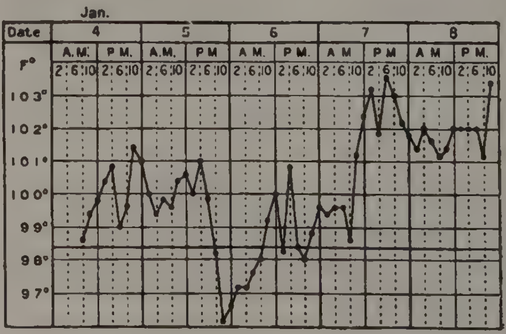

Fig. 76.—Two-hour chart of B——.

(3) *An Untreated Mixed Infection and Reinfection with Benign and Malignant Tertian Parasites.*

M. S., a native of India, aged 12 years. As in the two cases already described, malaria parasites were found in the blood of this boy in April, 1902. At this time the spleen was enlarged to the level of the umbilicus. The infection was with benign tertian forms. During the summer his spleen decreased considerably in size, and on November 1, when systematic examinations were begun, it was only three fingers' breadths below the costal margin. About this time he must have contracted an infection with malignant tertian parasites, for on November 1, when he was brought to me with a temperature of 102·6° F., a few malignant tertian rings were found but no benign tertian parasites. Until the beginning of December the infection appeared, from the results of blood examinations, to be only with malignant tertian forms, but on the 5th of this month benign tertian parasites were again found, and from that date the case must be considered as a mixed infection. The chart of temperatures taken twice daily is reproduced below (fig. 77).

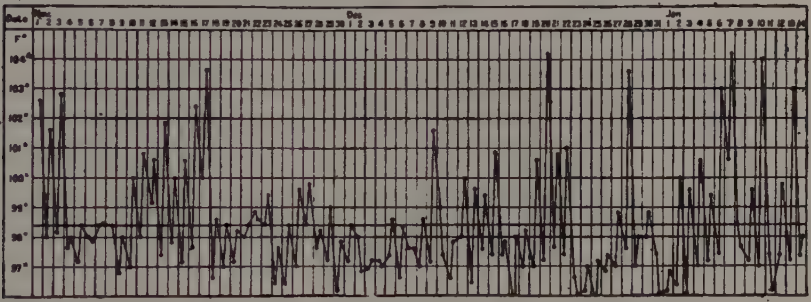

Fig. 77.—Chart of M. S.

In this case, the infection with malignant tertian parasites found in November was probably new, but it was known that the patient had suffered from an untreated infection with benign tertian parasites since the previous April, and throughout the summer his spleen had been enlarged nearly to the umbilicus. The chart and the results of daily microscopic examination showed that the infections were severe, but, as in the other cases, the illness was not continuous; it consisted of a series of attacks of fever, during which the boy was obviously ill, separated by intervals of apyrexia, during which, to a considerable degree, he recovered. On the whole it was not obvious at the termination of the systematic examinations in February, 1903 (by which time he had been under almost continuous observation for nearly a year) that his general condition was worse than it was when he was first seen. It was clear, too, that towards the end of the period of observation the attacks of fever were being felt with much less severity and that he was rapidly acquiring a tolerance to the effects of the parasitic invasion.

As regards diagnosis the chart is so characteristic that a diagnosis of "malaria" could have been made at almost any time by inspecting it; but in the absence of blood examinations the observer would have been much puzzled to state what type of parasite was the cause. Throughout the examinations only benign and malignant tertian parasites were found and therefore it is remarkable that the chart shows frequently a *quartan* type of fever. This is apparent during more than one period between December 8 and January 14, but nowhere as plainly as between January 7 and January 14. This portion of the chart is typical of a double infection with quartan parasites.

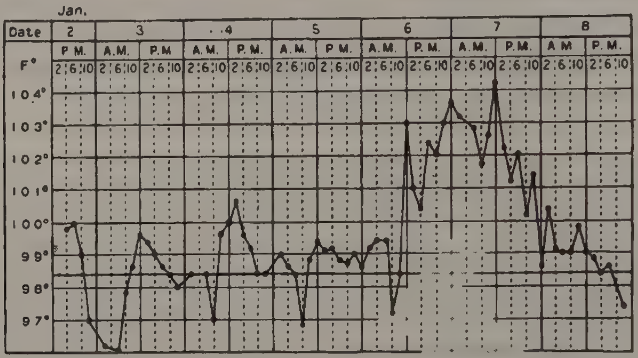

Fig. 78.—Two-hour chart of M. S.

The two-hour chart from the 2nd of January to the 8th which is reproduced above does not suffice to explain this, but it shows well the many sharp peaks of a temperature chart taken during a prolonged paroxysm (about forty hours) in which only malignant tertian rings, crescents, and pigmented leucocytes could be found in the peripheral blood.

The Developed Disease in Soldiers Invalided from Macedonia.

I have recounted the above cases in some detail because they give a truer clinical picture of the disease than can be observed in hospital patients who have usually received prophylactic or curative treatment with quinine. In such patients the course of the disease is seldom typical, and, particularly in many of the recent hospital cases from Macedonia, the problem is not malaria as it occurs in ordinarily healthy people, but malaria as it occurs in people who have been taking quinine almost continuously for weeks before, during, and after their attacks. In addition we are aware that many of the cases from Macedonia were a manifestation of EPIDEMIC MALARIA, not of the more usual endemic disease. It has already been mentioned that there are profound differences between these two forms of malaria, and the subject will be referred to again later in this chapter. Moreover it happened that most of the Macedonian infections were with both benign and malignant tertian parasites. In view of these unusual features it is remarkable how numerous were the cases which conformed in all essential respects with the classical types of malaria above described. Of the patients who were infected on the Salonika Front in the summer and autumn of 1916 and arrived in England during the following spring the great majority could not be classed in any sense as "chronic malaria" but were typical examples of the "developed disease" in its acute stages. The exceptional cases among these men will be noticed in Section III; the remainder presented the following chief features:—

(*a*) The persistent recurrence of relapses at intervals which were about the same as in the untreated cases of malaria which have just been described. The interval varied with each case but was fairly regular for any particular case; often it was about twelve or fourteen days.

(*b*) During each relapse the paroxysms of fever came on with great regularity at about the same time every other day, or every day, and the patients passed through the stages of "rigor," "heat" and "sweating" in a typical manner. The paroxysms were not very protracted (they seldom exceeded twelve hours) and in the great majority of cases they were not accompanied by unusually serious symptoms.

(*c*) The relapses were very amenable to quinine treatment; in many cases one dose of 15 grains of quinine, when given at the correct time, sufficed to cut short the relapse and to cause the parasites to disappear from the peripheral blood.

(*d*) Relapses for which no quinine treatment was given frequently underwent spontaneous cure after two or three paroxysms.

(*e*) On the afebrile days of a relapse patients usually felt well enough to desire to get up and go out of doors, and during the apyrexial intervals the improvement in the anæmic condition and in the general health was rapid. Splenic enlargement and tenderness were common during relapses, but, as a general rule, no splenic enlargement could be detected by palpation during the fever-free intervals.

As regards the great majority of the cases the following conclusions seemed to me justifiable: (1) Their primary infection had undoubtedly been with heavy doses of sporozoites; to this I attribute chiefly the large numbers of parasites usually to be found in the peripheral blood, and the frequency of the relapses. (2) There was no evidence that either the parasites or the human host had become habituated to quinine, but much evidence that the quinine treatment which the patients had received had been very efficacious in controlling the manifestations of the disease. This was shown by the comparatively small degree of anæmia, the absence of splenic enlargement, and other obvious differences between the condition of these cases and that of the untreated cases which have been described above. (3) By the time they arrived in England, which in many cases was about eight months after their primary infection, most of the patients already showed markedly that the infection was being overcome. This was clear both from the instances of spontaneous cure of relapses and from the observation that 10 grains of quinine given each morning sufficed, in the great majority of cases, to reduce the frequency and severity of relapses in an unequivocal manner.

GENERAL SUMMARY OF THE CLINICAL PICTURE.

The common clinical picture of malaria which, for diagnostic purposes, it is important to keep constantly in mind, may be outlined from the above account as follows: Malaria is always a disease of long duration, but is always an interrupted, not a continuous disease. Periods of fever and illness alternate with periods of apyrexia and partial recovery. During the pyrexial periods, if the temperature is carefully recorded every two hours over a sufficient number of days, the chart invariably shows both the intermittency and periodicity which are the essential clinical test of malarial fever. Provided that malaria is the only disease or condition from which a patient is suffering I doubt if any true case would fail to comply with this rule; but in applying it we must, of course, take into consideration cases of mixed infection and cases of "double" or "triple" infection.[1] Mixed infections with benign or malignant tertian parasites are most frequently met with, but combinations of benign tertian and quartan infection are also seen. Fig. 79 illustrates a mixed infection of this nature in a child. We must take into consideration also, that occasionally a paroxysm may come on before its proper time (when it is said "to anticipate") or may be delayed later than its proper time (when it is said "to postpone").

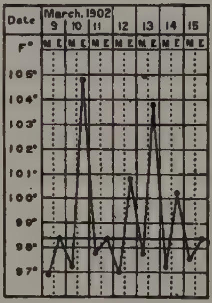

FIG. 79.

It is essential also to keep constantly in mind that a diagnosis of malaria cannot be excluded by finding that, at the particular period of a case when our diagnosis must be made, the symptoms and signs which are observed do not correspond with this common clinical picture. Likeness to the picture is of very great assistance, but to rely upon unlikeness—unless the case has been studied very closely at frequent intervals for several days—is to court disaster. This is true especially in regard to malignant tertian malaria which clinically and in the microscopic findings is so different from benign tertian and quartan malaria that some workers place its parasite in a separate genus.

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[1] "Mixed" infections must not be confused with "double" or "triple" infections. The latter terms are used to define infections with two or three groups *of the same species of parasite.*

During the apyrexial intervals freedom from subjective symptoms is a negative clinical test of great value which applies to both benign and malignant malaria. The patient is anæmic and may have an enlarged spleen, but as a rule he does not complain of feeling ill. His appetite is good, and under ordinary circumstances the weight which he may have lost during the attack of fever is quickly regained. Patients who have become somewhat accustomed to relapses usually begin again to carry on their ordinary occupation very shortly after the fever has left them. This quick disappearance of subjective symptoms is characteristic of malaria, and is very different from the protracted feeling of ill-health which follows recovery from even so short an illness as "sandfly fever."

USUAL TERMINATION.

In the great majority of cases of uncomplicated malaria the general course is towards recovery. Provided that a patient removes to a place where he is free from the risk of reinfection the disease almost never goes from bad to worse: instead it becomes less severe as time goes on and ultimately dies away. As a general rule a patient who has been infected on only one occasion suffers from very few relapses after the first six or eight months, though he may not be entirely free from a recurrence of short febrile attacks for two years or more. Persons who have been infected several times, or have contracted their infection during an epidemic period, suffer from more relapses and the disease lasts a longer time, but the general rule of gradually diminishing severity and ultimate recovery holds good.

Nowadays almost everyone who has overcome the primary stages of a malarial infection, but still suffers occasionally from a relapse, is careful to take quinine as soon as he realizes that an attack is about to begin. As a result of this early treatment it seldom happens that he is incapacitated for more than a day, or perhaps two days, and the temperature (when recorded) shows usually only one sharp rise and a rapid fall. I have kept continuously in touch with some of the more obstinately relapsing cases which arrived in England from the Balkans in 1917 and 1918. By the end of 1919, with a few exceptions which will be considered in the next Section, all were gradually throwing off their illness. The following history of a case of intense infection with both malignant and benign tertian parasites is representative of the majority: Pte. S. arrived in England from East Africa at the end of May, 1918. From June to December he had fourteen severe relapses, of which the first was with malignant and the remainder with benign tertian parasites. Early in 1919 he was demobilized and he returned to his civil occupation as a plumber. During the first six months of that year he had two severe relapses and several minor ones; but during the remainder of the year only three relapses in all. On November 4 he wrote: "I am getting better in that the relapses do not now come at regular intervals. Since August I have had two relapses which were severe enough to make me leave my work and go home. When I have an attack like that I take 15 grains of quinine and get to bed with a few good hot drinks and sweat it out, but it leaves me very weak for at least forty-eight hours. Then I take 15 grains of quinine daily for four days after each attack." At an examination in March, 1920, he appeared in robust health, but he said that he had had a slight relapse a few weeks previously.

CHRONIC MALARIA.

Persons who are repeatedly infected and reinfected often fail to make a sufficient recovery between their frequent attacks, and the result is that they pass into a condition which is correctly named "chronic malaria." Until about fifteen years ago the signs and symptoms of this condition were incorrectly described. The error arose from the assumption that a disease which natives of India were accustomed to call *kala-azar* was a manifestation of chronic malaria—that it was in fact "malarial cachexia." The consequence was that the *kala-azar* syndrome (which includes fever, anæmia and great enlargement of the spleen) came to be described as the syndrome of chronic malaria or "malarial cachexia." This description was quite different from the clinical description of comparatively recent malarial infections. It represented the patient as suffering continuously from irregular fever (of the type shown in fig. 80) which was not amenable to quinine: and to the physical signs of enlargement of the spleen and liver and a dark "earthy" colour of the skin, were added emaciation and a condition of continuous and progressive ill-health usually terminating in death.

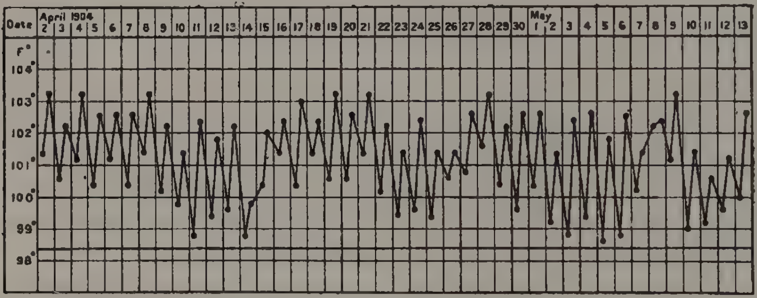

FIG. 80.—Chart of a case of kala-azar.

The discovery that *kala-azar* is a disease quite separate from malaria made it necessary to revise our conception of what had been called "malarial cachexia." It is now realized that "cachexia" is only exceptionally an accurate term to apply to the condition of patients who have suffered for a long time from repeated malarial infections and reinfections. Such patients are in a chronic condition of severe anæmia and their spleens may extend to the umbilicus, or lower, but as a rule they are not emaciated, and as a rule they are not incapacitated, in their fever-free intervals, from carrying on their usual work. During the intermittent febrile attacks from which they suffer a carefully recorded temperature chart shows the same characters as in relapses of more recent cases, and by this means and examination of the blood a diagnosis can be made with almost the same facility as in recent cases. Above all the illness does not tend, even when untreated, to go from bad to worse; instead it nearly always happens that when these patients are removed from the risk of repeated infection they speedily recover. Cases of true acute malarial cachexia will be described in Section III. It will be found that they represent a type of disease very different from the type represented by this description and therefore very different from the disease to which the term "malarial cachexia" was formerly applied.

In some recent articles the term "chronic malaria" has been applied to the later stages of the primary infections which were contracted during the War. I include these stages in the description of "the developed disease" and reserve the term "chronic malaria" for cases due to constantly repeated reinfections during successive years while the subject remains in the endemic area.

CHAPTER VII (*continued*).

SECTION II.

FURTHER CLINICAL DETAILS AND AN ACCOUNT OF THE PATHOLOGY.

This Section contains further clinical details of the many symptoms and signs which have been commonly or rarely observed in cases of malaria, and an attempt is made to describe briefly the morbid changes and pathology which are usually associated with certain features of the clinical picture. But it must be noted that although, as a rule, we can correlate the most striking phases of the malarial syndrome with definite macroscopic and microscopic changes in the blood and tissues, we are still unable to do more than conjecture by what pathological process some of the symptoms arise. In particular it is difficult to state the relative importance of the rôles played by (1) the purely mechanical effects of the parasitic invasion, such as destruction of red cells, blocking of capillaries, &c.; (2) the flooding of the blood plasma with foreign matter, such as corpuscular debris, malarial pigment, free malarial parasites (merozoites), &c.; (3) the various toxins which it is believed are elaborated by the parasite during its growth. We can, of course, observe the direct pathological process by which, for example, a parasite destroys the red cell in which it lies, or a clump of parasites blocks a capillary, but we can only guess at the indirect process by which, for example, a severe parasitic infection is followed by a persistent lowering of the peripheral blood-pressure.

For purposes of reference to particular headings in this section I preface it with the following brief synopsis :—

(1) THE FEVER, p. 130.—Its intermittency and periodicity; its onset shortly after the commencement of sporulation of the parasite : the usual pathological explanation of the fever; the causes of atypical charts; the influence of improper quinine treatment; so-called "quinine fever" and "quinine-resisting" fever; the relation and lack of relation to the number of parasites; "paradoxical fever."

(2) SYMPTOMS ACCOMPANYING THE FEBRILE PAROXYSM, p. 133.—The view that the "chill," vomiting, headache, &c., are manifestations of an anaphylactic process.

(3) THE ANÆMIA, p. 133.—Its cause and degree; diagnostic value; severity in inadequately treated cases.

(4) THE BLOOD CHANGES, p. 134.—(*a*) The red blood corpuscles; (*b*) the leucocytes; (*c*) splenic and other unusual cells in the peripheral blood; (*d*) phagocytosis; (*e*) changes prior to the onset of the paroxysm; (*f*) the hæmoglobin; (*g*) the pigments.

(5) ENLARGEMENT OF THE SPLEEN, p. 138.—In acute cases: in chronic cases; effect of quinine treatment; rarity among malarious soldiers returned from the Eastern war areas; great enlargement in untreated cases of indigenous malaria in England and in the tropics; morbid anatomy and pathology.

(6) **Enlargement of the Liver**, p. 139.—Common in all forms; the morbid anatomy and pathology; occasional fatty degeneration.

(7) **The Digestive System**, p. 139.—Affected in all cases; cause of digestive disturbance; cause of vomiting; intestinal changes; hæmorrhages.

(8) **The Nervous System**, p. 140.—Nervous symptoms in acute and chronic cases; serious "cerebral malaria"; changes in the mental condition (malarial psychoses); affection of the vasomotor centres; the causes of symptoms referable to the nervous system.

(9) **The Circulatory System**, p. 141.—Symptoms referable to the heart; the marked effect of malaria upon the blood-vessels; tendency to hæmorrhage; loss of vascular tone and the low blood-pressure; pathology; heart changes; causes to which the low blood-pressure is attributed.

(10) **The Urinary System**, p. 143.
(11) **The Respiratory System**, p. 143.
(12) **The Skin**, p. 143.
(13) **The Muscular System**, p. 144.
(14) **The Suprarenal Glands**, p. 144.

(1) THE FEVER.

In malaria the fever, in typical cases, is of a definite and peculiar type, the distinctive characters of which are *intermittency* and *periodicity*. Intermittency means that the fever ceases at intervals; the temperature alternately falls to normal or below, and rises again. Cases of malaria due to the benign tertian and quartan parasites so constantly exhibit this type of fever that they are usually called simply "the intermittent fevers." Periodicity means the habitual tendency of the fever to recur at stated intervals of time. Thus the fever may recur at intervals of twenty-four hours (quotidian periodicity), or at intervals of forty-eight hours (tertian periodicity), or at intervals of seventy-two hours (quartan periodicity). Microscopic examination of the blood during the course of the illness shows that the intermittent and periodic characters of the fever are coincident with certain stages of growth and multiplication of the malaria parasites in the peripheral blood and internal organs of the patient. It has already been described how, in the red blood corpuscles of man, the malaria parasites grow larger and larger until they attain their full size, when they divide up into a number of merozoites which burst through the thin remnant of the corpuscle and become free in the blood plasma ready to enter other corpuscles. If the blood of a patient suffering from one of the typical intermittent fevers is frequently examined, it will be found that, during the period taken by the parasite to grow to its full size in the red corpuscles, the patient does not suffer from fever or other very obvious symptom, but that as soon as some of the parasites divide up and burst from the red cell in the act of "sporulation" the attack of fever begins.[1] It is usual to explain the occurrence of fever at this particular stage by assuming that while the parasite is growing inside the corpuscle and feeding upon its hæmoglobin it is also manufacturing and storing up in its body a pyrogenetic chemical substance, but that so long as the parasite remains enclosed in the envelope of the red blood corpuscle, this substance does not escape into the plasma and cause its toxic effect. When, however, the parasite bursts from the red cell in the act of "sporulation" the chemical substance is liberated into the plasma, reaches the pyrogenetic centre in the nervous system, and so exerts its fever-producing influence. On this view it will be clear that a parasite which takes twenty-four hours to grow to its full size and sporulate must cause an attack of fever every day (quotidian fever); one which takes forty-eight hours must cause an attack every other day—which is the same as saying every two days or every third day (tertian fever); and one which takes seventy-two hours must cause an attack every fourth day—which is the same as saying every three days—the fever-free interval between each attack being of two days' duration (quartan fever). It will be apparent also that if a parasite, for some reason or other, completes its growth and division in a shorter period than twenty-four, forty-eight or seventy-two hours, a different clinical type of fever will result; and also that a different clinical type may be caused by the presence in the blood of two or more groups of parasites which sporulate at different times, or at the same time on different days. If, for example, a patient were infected with two groups of the benign tertian parasite, one group being due to sporulate at 10 a.m. on the first, third, fifth, &c., the other group being due to sporulate at 10 a.m. on the second, fourth, sixth, &c., the patient would have a paroxysm of fever at 10 a.m. every day and his temperature chart would be described as being of the "double tertian type." Similarly it can easily be worked out that a daily paroxysm of fever might be due to an infection with three groups of quartan parasites ("triple quartan"), or how it might be due to a *mixed infection* with two, or perhaps with all three species of the parasite, or how the presence of several groups of parasites of the same or different species, which are due to sporulate at various times, may produce irregular charts in which the intervals between the paroxysms are not clearly marked. In such cases the paroxysms overlap one another and the fever, instead of being intermittent, may be remittent or even (for a short period) almost continuous. Moreover, it must be remembered that even when an infection is with only one group of parasites, the temperature chart may be atypical from one or other of the following causes. The first is that sometimes, for no obvious reason, the day of fever changes abruptly. This is rare in quartan fever (which is remarkable for the regularity with which the febrile paroxysms recur on every fourth day at the same hour) but is common in both benign and malignant tertian fever. The second is the lesser degree of change known as anticipation or retardation of the time of day at which the paroxysm occurs. This is commonest in malignant tertian, but occurs also in benign tertian infections. The third is the tendency (seen only in malignant tertian infections) for some of the individual parasites of a particular group to complete their cycle quicker than others. Not all observers agree that this happens, but it accords best with the clinical and microscopical findings in the very protracted paroxysms (thirty to forty hours or more) which sometimes occur in a severe malignant tertian infection (see fig. 81 below).

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[1] In quartan fever (in which the asexual cycle of the parasite is passed chiefly in the peripheral blood) sporulation can be observed to occur some little time before the onset of the cold stage, and it can be seen that some of the young merozoites have already entered new corpuscles before the hot stage has passed.

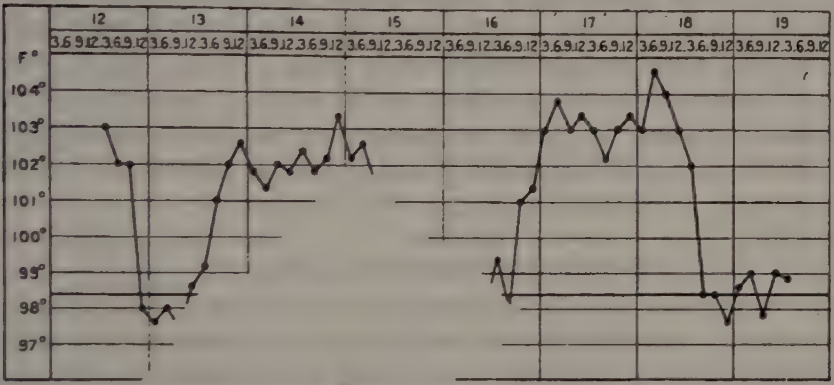

Fig. 81.—Malignant tertian fever with protracted paroxyms and short fever-free intervals (after Craig).

The fourth and by far the most frequent cause of atypical temperature charts is inadequate, or otherwise improper, treatment with quinine. It is a good rule that as regards untreated malaria the temperature chart, when carefully recorded at frequent intervals, always shows clear signs of becoming intermittent and periodic within a few days after the onset of the illness; but this diagnostic sign is seldom apparent in patients who have been treated with quinine in small doses, or at irregular times, or when their digestive system is out of order. Chart 67, on p. 113, shows an example of a case in which it was found, some time after admisssion to hospital, that the patient was receiving quite insufficient doses of quinine; and during the war numerous examples occurred in which moderate doses of quinine made the fever irregular, but did not cause it entirely to disappear. By some observers these cases were thought to be examples of what is termed secondary or "quinine fever," but when care was taken to ensure that the drug should be properly absorbed, it was found that most of them could be more correctly classed as instances of "quinine-resisting" fever.

In view of the effect of quinine in changing the character of the temperature chart, and because it is seldom or never possible to find malaria parasites in the peripheral blood of a patient under quinine treatment, it is very important to be sure of our diagnosis of malaria before we decide to commence treatment with that drug.

In primary untreated cases of malaria and during many of the early relapses, we can usually correlate approximately the occurrence and degree of fever with the number of asexual parasites which can be found in the peripheral blood.[1] Later in the disease and in cases of repeated infection and reinfection this is not often possible; and we may have, on the one hand, persons who show many parasites in their blood without having fever or other obvious symptoms of malaria ("apparently healthy malaria carriers"); and, on the other hand, patients who are clearly suffering from a febrile attack of malarial origin, but in whose peripheral blood few or no malarial parasites can be found by ordinary routine methods of examination (so-called "paradoxical relapses"). These occurrences show that the relationship of the presence of parasites in the blood to the occurrence of fever is not necessarily so simple as it is usually thought to be.

(2) SYMPTOMS ACCOMPANYING THE FEVER.

The "cold," "hot" and "sweating" stages of a typical malarial paroxysm were described on p. 115 of Section I, and the heading is repeated here only for the purpose of noting the recent view (which is of course hardly more than a conjecture) that the malarial paroxysm is in part an anaphylactic process. It is said that the symptoms accompanying the fever are a consequence of an anaphylactic or "hæmoclastic" shock caused by the sudden entry into the plasma of burst parasites which act as a foreign colloidal substance. Abrami and Senevet have given the name "hæmoclasis" to the phenomena resulting from inoculation of certain foreign substances, and, noting that they are very similar to the phenomena of the malarial paroxysm, they suggest that a similar determining factor may be concerned. The usual signs of hæmoclasis are: a lowered arterial tension, leucopenia, alteration of the differential leucocyte count, diminution in the number of red cells, and changes in the coagulability of the blood. They have ascertained that benign tertian malarial paroxysms are preceded by a hæmoclastic crisis evidenced by these signs (see the table on p. 137). They regard the "chill," the vomiting, the headache, the backache and other symptoms of the cold stage of the malarial paroxysm as manifestations of this hæmoclastic shock.[2]

(3) THE ANÆMIA.

No one can pass through even a single attack of malaria without becoming temporarily anæmic, for rapid destruction of red blood corpuscles is a constant phenomenon in the disease. In addition to the destruction of infected corpuscles by the parasites which they contain, many infected and uninfected corpuscles are destroyed by phagocytosis in splenic "endothelial" cells, and in some cases many are destroyed by hæmolysis. In primary attacks the loss of red blood corpuscles during each febrile paroxysm may be from a quarter of a million per cubic millimetre of blood to a million or more. The white blood corpuscles are also reduced in number and there is a great fall in the amount of hæmoglobin.

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[1] See especially a paper by Ross and Thomson in the *Annals of Tropical Medicine and Parasitology*, vol. iv, No. 3, p. 267, and another by Thomson in the same publication, vol. v, No. 1, p. 57.

[2] P. Abrami and G. Senevet in the *Bulletin de la Société Médicale des Hopitaux de Paris*, No. 19, June, 1919, pp. 530 and 537.

In consequence of these blood changes, patients who have passed through a paroxysm present a marked pallor which contrasts strikingly with their normal appearance. The pallor of the skin in malaria may also be correlated in part with the hyperæmia of the internal organs. The rapid onset of anæmia is an important diagnostic sign which not infrequently leads to the detection of malaria in persons who may not have complained of anything more definite than a feeling of "chilliness" or of "being out of sorts." In England it has led to the discovery of several cases of malaria among school children. During the apyrexial intervals the blood tends quickly to become normal again, especially if quinine treatment has been begun early in the course of the illness. Patients, however, who have suffered from a number of relapses which have been inadequately treated, develop a condition of intense anæmia which persists for a long time. The blood of such patients is often so thin and watery that it is difficult to spread it on a slide and, in addition to an intensely pale, sallow complexion, they present many secondary symptoms which are due essentially to the anæmic condition of their blood. A considerable number of cases of this kind occurred among European soldiers (especially in the French army) during the war. The total count of red blood corpuscles is usually below three million per cubic millimetre of blood and may be below one million. In a few cases the condition is refractory to treatment, and death from this "pernicious anæmia" sometimes occurs. (See Section III.)

The presence of anæmia should be ascertained by examining the mucous membranes of the eyelid, lips, and mouth, rather than by an inspection of the skin, and in doubtful cases (especially in dark-skinned races) the hæmacytometer and hæmoglobinometer should, of course, be used.

(4) THE BLOOD CHANGES.

In addition to the parasitic infestation which has already been described, the blood changes in malaria are briefly as follows:—

(*a*) *The Red Blood Corpuscles.*—The loss of red cells in an acute attack of malaria may be a million or more per cubic millimetre of blood within as short a period as twenty-four hours. As a rule the reduction is greater in malignant tertian than in benign tertian and quartan infections. A reduction occurs with each paroxysm, but it is greatest during the first two or three paroxysms. During the apyretic intervals the number of corpuscles rapidly increases. The loss is due partly to the destruction of the red blood corpuscles by the parasites which they contain, partly to the engulfment of infected and often non-infected corpuscles by phagocytic cells in the spleen. In the condition known as blackwater fever the reduction is due to the solution of red cells in the plasma, probably by the action of a hæmolytic toxin.

The changes in size and staining reactions of red cells which are invaded by parasites have already been described.

(*b*) *The Leucocytes.*—In malaria there are changes in the total number of leucocytes present in the peripheral blood and in the relative proportions of different varieties.

As regards total number, the general rule is that within a few hours of the onset of an attack a marked leucopenia occurs, the number of leucocytes being generally between 3,000 and 5,000 per cubic millimetre of blood instead of about 8,000 or 9,000, and the ratio of white corpuscles to red changing during the apyrexial interval from the normal of about 1 to 500 to perhaps 1 to 900. It is important to remember, however, that sometimes in the course of the disease there may be an increase in the total number of leucocytes. For example, a true leucocytosis is by no means infrequent during the very early stage of an ordinary acute attack (especially in malignant tertian infections) and for a longer period in pernicious cases while the fever is rising.

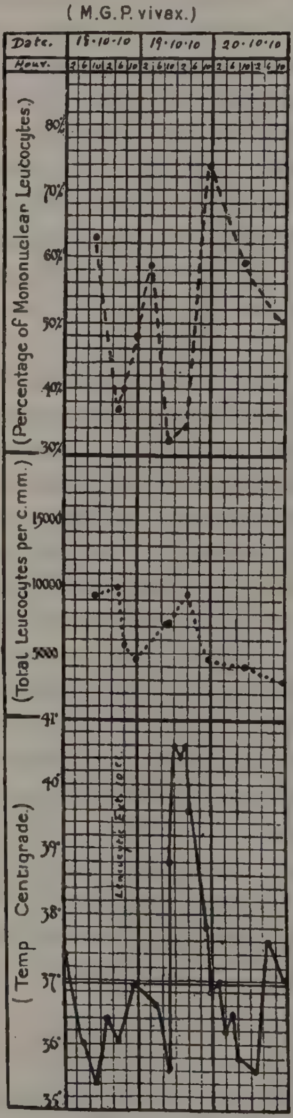

FIG. 82.

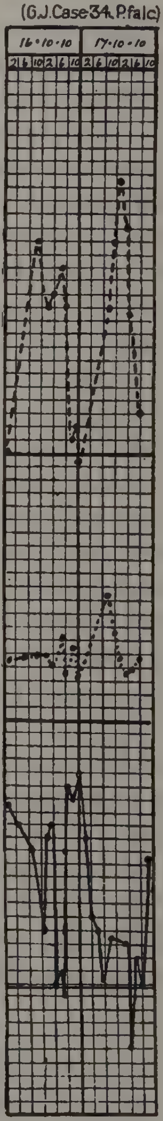

FIG. 83.

David Thomson has also described very completely the transient "post-malarial" leucocytosis which sometimes occurs every day in malarial patients who have been treated with quinine.

As regards the changes in the relative proportions of the different varieties of leucocytes, the general rule is that during the apyrexial interval the polymorphonuclear leucocytes fall from the normal of about 70 per cent. to about 50 per cent., and the mononuclear leucocytes (all forms) rise from about 25 to about 45 per cent. of the number of leucocytes observed. "The mononuclear percentage varies inversely with the temperature. When the temperature is rising the number of mononucleated leucocytes in the peripheral blood is falling; and when the temperature falls the mononuclears increase. The greatest number are found in the period between the paroxysms, when they quite frequently rise as high as 80 per cent. of the total leucocytes." (Thomson in the *Journal of the Royal Army Medical Corps*, vol. xxviii, p. 671.) The accompanying diagrams (figs. 82 and 83) taken, by permission, from Captain Thomson's paper, sufficiently illustrate these points.

The mononuclear leucocytes referred to include (1) small lymphocytes, (2) large lymphocytes, (3) intermediate lymphocytes, (4) other large mononuclear leucocytes. The increase is chiefly in the large varieties of these cells, but observers differ so greatly in their identifications of the various kinds of mononuclear leucocytes that it is probably best to group all mononuclear leucocytes together.

(*c*) *Other Cells which may appear in the Peripheral Blood.*—The changes just described relate to white cells of the varieties ordinarily present in normal blood. Another change, more important from the diagnostic point of view, is the entry into the peripheral blood of certain cells which are absent from, or very rare in, the blood of healthy subjects. Of these cells the type most frequently present in the blood of malaria patients is a macrophage of 15 or more microns in diameter. It may be bluntly oval or more or less circular in shape. The protoplasm is hyaline. In the oval forms the nucleus is kidney-shaped and placed excentrically; in the circular forms it is more rounded and usually central. A rarer type in the peripheral blood is a still larger cell which probably has been desquamated from the vascular endothelium. The nucleus is large and of irregular shape. The protoplasm is hyaline and may be vacuolated. Malaria pigment, red blood corpuscles and the debris of corpuscles and of parasites may be found in both the macrophagocytic and endothelioid cells.

(*d*) *Phagocytosis.*—The malarial pigment and the detritus of parasites and red blood corpuscles are taken up by the leucocytes (except the small lymphocytes) and by the macrophages just described. A considerable removal of red corpuscles (both infected and non-infected) from the circulation by phagocytic cells takes place in the spleen and is perhaps a chief cause of the anæmia, but in some cases the loss of red cells is so great and so rapid as to suggest that in addition there is a solution of red cells in the plasma.

(*e*) *Changes prior to the Onset of the Paroxysm.*—With the reservation that, so far as I am aware, the observations have not yet been confirmed, it is worthwhile to mention here the remarkable blood changes which Abrami and Senevet have described as occurring from one to three hours before the onset of a benign tertian malarial paroxysm. The changes are a gradual diminution in the numbers of white and red cells, an inversion of the normal differential leucocyte count, a lowered arterial tension, and a change in the coagulability of the blood. It is said that the total leucocyte count commences to fall about two hours before the onset of the cold stage, and within an hour may be as low as 2,000 per cubic millimetre: thereafter it rises rapidly and at the time of onset of the cold stage may be as high as 12,000 or 15,000. The following table gives details of the changes observed:—

Time	Blood-pressure		Total leucocyte count	Differential leucocyte count		Red blood corpuscles	Coagulability	Temperature Centigrade
	Maximum	Minimum		Polynuclear	Mononuclear			
7.0	14·5	9	9,400	67	31	+++	18·5	..
7.15	14·5	9	..	..	..	..	..	36·9°
7.30	14	9	10,000	..	..	..	..	..
7.50	13	9	6,000	62	36	++	12·0	..
8.0	12	8	..	..	..	..	6·5	..
8.10	11	8	4,800	52	47	+	..	36·9°
8.20	11	8·5	3,000	..	..	..	7·0	..
8.30	12	9	2,000	44	50	+	..	..
8.40	14	9	2,600	..	..	..	..	..
8.50	14·5	9	6,000	56	39	++	17·0	..
9·0	16	9	9,000	..	..	..	..	..
9.15	15·5	9	11,000	..	..	..	18·5	..
9.30	18	9	13,000	73	23	+++	..	36·9°
9.43	19·5	9	Onset of cold stage		..	..	..	38·4°

(*f*) *The Hæmoglobin.*—The reduction in hæmoglobin corresponds as a rule to the reduction in red blood corpuscles, but the hæmoglobin value seldom returns to the normal standard so quickly as does the number of corpuscles. This is shown in the following diagram (fig. 84).

(*g*) *The Pigments.*—The true malarial pigment ("melanin" or "hæmozoin") is first seen as black or brown rods, granules, or blocks, in the parasites contained in red blood corpuscles. When the parasites escape from the corpuscles the pigment is taken up by the leucocytes and other phagocytic cells, and becomes distributed in all the tissues of the body, but chiefly in the spleen, liver, brain and bone-marrow. This pigment is found in no other disease than malaria. Quite another variety of pigment, called *Hæmosiderin*, is also present in malaria as well as in other diseases associated with blood destruction. It is yellow in colour and is found not in the

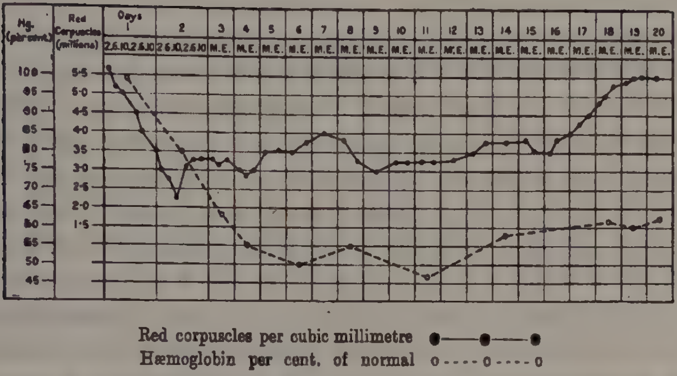

FIG. 84. (After Ziemann.)

blood-stream but in the liver, spleen and other viscera. It is insoluble in caustic potash and gives an iron reaction when treated with ferrocyanide of potassium and hydrochloric acid. The true malarial pigment, on the other hand, is soluble in alkalies and no trace of iron can be demonstrated in it.

(5) ENLARGEMENT OF THE SPLEEN.

Next to fever and anæmia the most frequent physical sign in malaria is enlargement of the spleen. During each febrile attack the organ becomes hyperæmic, painful, tender and swollen, and in practically every case of untreated malaria its edge can be felt on palpation a few days after the onset of definite symptoms. This acute swelling occurs before there can be any inflammatory changes in the splenic tissue, and is due mainly to distension with blood as a result, perhaps, of the lowered vascular tone which is most marked in the blood vessels of the abdominal region. In chronic relapsing cases which have had little or no treatment with quinine, the spleen often forms a large tumour reaching a hand's breadth or more below the costal margin and quite frequently to the umbilicus. When patients are treated with quinine at a fairly early stage of the disease the enlargement quickly subsides. This is probably the reason why it is comparatively rare to find a palpably enlarged spleen among malarious soldiers who have returned to this country from the Eastern war areas. In marked contrast to this, we have found in England very large spleens among children who have contracted the disease locally through the agency of such soldiers and whose cases have remained undiscovered for some days or weeks. Among the inhabitants of malarious localities in the tropics, where quinine is not readily available, the percentage with greatly enlarged spleens is often fifty or more, and often approaches 100.

In early acute cases, tenderness over the splenic area (sometimes due to perisplenitis) can often be elicited before actual enlargement can be detected. It is easier to demonstrate enlargement in children than in adults, and it is sometimes easier to demonstrate it by percussion than by palpation. It is best to percuss forwards from a base line drawn from the middle of the axilla to the trochanter.

Pathology.—The spleen has a tendency to filter off the parasite-infected corpuscles from the blood which passes through it, and it is the source of many of the macrophages and other phagocytic cells. Hence parasites and malarial pigment are usually very abundant in it and can often be found when not sufficiently numerous to be detected in the peripheral blood. The chief microscopic appearances in smears or sections of a malarial spleen are: (*a*) red blood corpuscles containing parasites in various stages of development; (*b*) a large number of phagocytic cells including giant macrophages and endothelial cells; (*c*) an abundance of true malarial pigment occurring as granules, rods, blocks or masses in the phagocytic cells and also free in the venous sinuses; (*d*) golden yellow pigment (hæmosiderin) derived from destroyed red corpuscles; (*e*) evidence of phagocytosis of red blood corpuscles; (*f*) thrombosis of capillaries; (*g*) local necrosis of the splenic pulp; (*h*) congestion and distension of the splenic sinuses with blood.

(6) ENLARGEMENT OF THE LIVER.

This is also a frequent sign in acute malaria. It is usually accompanied by tenderness and often slight jaundice. It occurs quite commonly in the benign tertian and quartan types of the disease as well as in the more severe malignant tertian variety.

Pathology.—The morbid changes in the liver are nearly as numerous as in the spleen, but parasites are less abundant. Besides enlargement, pigmentation and great congestion, the chief changes are seen in the capillaries, the liver cells and the connective tissue. The capillaries are distended with macrophages, endothelial cells and true malarial pigment. The liver cells may be atrophied or necrosed and often contain much yellow pigment (hæmosiderin). Fatty degeneration of the central areas of the liver has been accorded by Dudgeon and Clarke in fifteen out of a total of fifty-one fatal cases of malignant tertian malaria examined, and fatty globules in the liver cells were found by Christophers in fatal cases of blackwater fever.

(7) THE DIGESTIVE SYSTEM.

The digestive system is affected in all cases of malaria. At the onset of an attack the mouth becomes dry, the tongue thickly coated, and the appetite is lost. Nausea is almost always troublesome and in many cases there is severe vomiting, which may be either simple or of a "bilious" character. In ordinary cases constipation is the rule, and this together with the congestion and sluggish action of the liver sometimes leads patients to diagnose mild relapses as "a bilious attack," or "a touch of liver." Diarrhœa (which is occasionally of a choleraic type) and hæmorrhage from the bowel are complications in some severe infections. Acute splenic pain is sometimes referred to the region of the appendix and in rare cases the sudden onset of intense pain in the upper abdomen followed by collapse and signs suggesting acute peritonitis has been found to be due to acute malarial pancreatitis.

Pathology.—Deficient gastric secretion is said to be the common cause of the usual digestive disturbances and is one of the causes of diarrhœa. But the persistent vomiting which often ushers in the febrile paroxysm can seldom be due to a local gastric condition. It may be a consequence of the cerebral anæmia which follows the rush of blood to the abdominal organs; or, as has already been mentioned, it may be a manifestation of an anaphylactic process. When there is a special localization of an infection in the intestines, the capillaries of the mucosa and villi will be found to be blocked with red corpuscles containing parasites in all stages of growth and with leucocytes and other phagocytic cells containing masses of pigment. Small hæmorrhages into the tissues of the mucosa and villi and patches of necrosed epithelium may be present. There may be a massing of parasites in the capillaries of the pancreas with small hæmorrhages and deposits of malarial pigment in the pancreatic tissue.

(8) THE NERVOUS SYSTEM.

Even in the "benign" forms of malaria some symptoms referable to the nervous system are usually present. Just prior to the onset of an attack, patients often feel anxious, apprehensive and depressed. During the hot stage of the febrile paroxysm delirium is common. Frontal and occipital headache is present in nearly all cases; and neuralgia, usually unilateral, may be a troublesome symptom. Pain in the back and aching of the bones are often acute. In some chronic cases there are severe pains referred to particular nerves or particular areas of nerve supply, e.g,, the supraorbital area. In such cases detailed examination may show that certain areas of the body corresponding to the cutaneous distribution of the nerves from some segments of the spinal cord are unusually sensitive to light pin-pricks. Dr. Carmalt Jones detected the presence of such hyperalgesic areas in eighty-three out of 120 cases of malaria examined, but he also found similar areas in sixty-eight out of seventy-three cases of trench fever.

In intense infections, particularly with the malignant tertian parasite, serious cerebral symptoms are often present, notably drowsiness, delirium, stupor and coma, not infrequently terminating fatally. Other very serious nervous symptoms occurring during periods of epidemic prevalence are aphasia, paraplegia, hemiplegia, convulsions, epileptiform seizures, uncontrollable sweating, and hyperpyrexia.

Temporary or prolonged *change in the mental condition* is in some cases an important result of malarial infection. The manifestation in many cases is a mental confusion, with dullness, apathy, and loss of memory; in other cases it is a condition of restlessness, anxiety and tremors with sleeplessness and hallucinations; in others there is acute mania; in others melancholia.

Meningitis, peripheral neuritis and general paralysis are other conditions which have been ascribed to malaria. These and other exceptional nervous manifestations of the disease will be referred to more fully in the paragraphs dealing with complications and *sequelæ.* (See pp. 153, 155 and 164-165.)

Affection of the nerve centres controlling the vasomotor mechanism is indicated during the febrile paroxysm in the stages of "chill," and "heat"; during the apyrexial intervals it is indicated by a chronic condition of coldness and lividity of the extremities. In very anæmic patients the condition may be accompanied by some œdema of the tissues.

Pathology.—Some of the malarial symptoms referable to the nervous system are due to the mechanical effects of a massing of parasites and pigment in the cerebral capillaries, others to the action of toxins which cause degeneration of nerve cells and tissue, and degeneration of the endothelial lining of vessels resulting in punctiform hæmorrhages into the nerve tissue in their neighbourhood. In comatose cases which have ended fatally it is usual to find that the capillaries and small arterioles are blocked with numerons red cells containing parasites often in the sporulating stage. Parasites apparently not in red blood cells are also found, and numerous pigmented leucocytes, macrophages and endothelial cells, as well as much free malarial pigment. The parasite-infected corpuscles have a tendency to cling to the sides of the vessels and in severe cases there is complete occlusion and thrombosis. There may be small hæmorrhagic patches round the blood-vessels. The nerve ganglion cells show signs of degeneration by their abnormal shape, the disappearance of the chromatic bodies of Nissl, granulation of the protoplasm, and loss of chromatin in the nucleus.

It is important to realize, however, that profound symptoms of "cerebral malaria" may occur in the absence of definite histological changes of the above character. This is clear from the quick recovery which in many serious cases follows energetic quinine treatment, as well as from the occasional failure to find definite lesions in the brain of patients who have died from what is called "cerebral malaria." In these cases we must assume that the symptoms are due to a profound toxæmia.

(9) THE CIRCULATORY SYSTEM.

In the great majority of cases of malaria there are few or no symptoms indicating that the heart is affected, but in many of the intense infections which have occurred during the War, weakness and dilatation accompanied by precordial pain, palpitation, fainting attacks, and syncope have been by no means uncommon. In chronic cases tachycardia may be present and may persist for a considerable time. Dr. Carmalt Jones, from war experience in Egypt, reported that in his opinion malaria is liable to produce greater evidence of myocardial change than most of the other contributory causes of disordered action of the heart. He found definite increase in the area of cardiac dullness and valvular murmurs more frequently in malarial subjects than in those whose disability was due to uncomplicated physical strain, neurasthenia, gas poisoning, or trench fever.

Malaria has a marked effect upon the blood-vessels, both indirectly through its action on the vasomotor nerves and directly by the action of the parasites on the vascular tissue cells. Bleeding from the vessels in the mucous membrane of the alimentary canal, especially the bowel, is by no means a rare complication of the disease, and it occurs also in other regions. In the case of indigenous malaria in England recorded on p. 112, profuse bleeding from the mouth and nose was the first symptom which attracted attention. Small hæmorrhages in the central nervous system, especially in the region of the cortex, are a cause of symptoms of "cerebral malaria" in some cases.

Loss of vascular tone is constant in malaria. Even during the "hot" stage of an acute attack the minimum blood-pressure (which represents the true arterial tension) is much below normal, although the maximum pressure may be somewhat increased. The diminution of the blood-pressure is greatest shortly after the febrile attack, but persists throughout the apyrexial intervals between the relapses even when these intervals are of several weeks' duration. The average pressure readings for a strong healthy man should show a maximum of about 120 mm. Hg and a minimum of about 80 mm. Hg; but, according to Plehn,[1] in many soldiers who contracted malaria in Macedonia during the War the maximum pressure reading was usually not more than 80 or 90 and the minimum between 40 or 50, or even less.

Pathology.—It is rare to find any characteristic change in the heart of patients dying from malaria, and in all probability the low blood-pressure should not be regarded as a sign of cardiac weakness. In fatal cases of malaria, death usually results from paralysis of the respiratory centre, but there are, of course, exceptional cases, and recently Dudgeon and Clarke[2] have drawn attention to some fatal cases in which they found diffuse fatty degeneration of the heart "similar in all respects to that which has been found in acute diphtheritic toxæmia." They note that the cases occurred during the summer of 1916 in Macedonia, when the parasites were acting on men unaccustomed to a prolonged period of hot weather and under military conditions which prevented adequate rest being obtained. Of forty-five cases of fatal malaria in which the cardiac muscle was examined slight fatty degeneration was found in fifteen, moderate in three, and diffuse in five. In seven cases the cardiac capillaries were found to be loaded with parasites, and thrombosis of the vessels was noted in two cases.

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[1] Plehn in the *Muenchener medizinische Wochenschrift*, February 7, 1919, p. 146.

[2] The *Quarterly Journ. of Med.*, vol. xii, No. 48, July 1919, p. 372.

The clinical picture associated with the condition of diffuse fatty degeneration is one of acute cardiac failure. It will be referred to again in the account of the complications of malaria.

The fall of blood-pressure in malaria is attributed by some writers to a specific action of the parasites on the vasomotor nerves; by others it is considered to be a manifestation of an anaphylactic process; by others it is thought to be due to a lesion of the suprarenal glands.

(10) THE URINARY SYSTEM.

The passing of a large amount of urine frequently precedes or ushers in the febrile paroxysm, and polyuria may be present throughout the attack and extend into convalescence. The urine during the early stage of an attack is usually pale; later it is high-coloured and shows a heavy sediment of urates and phosphates. The amount of urea is increased appreciably above the normal and in severe cases the colour may be very dark from the presence of bile pigments. Temporary albuminuria is frequent especially towards the end of the febrile paroxysm, and in severe malignant tertian infections epithelial and granular casts may be present.

The changes which occur in hæmoglobinuria will be mentioned in the description of that complication.

Nephritis is one of the less common complications of malaria and in rare cases may be of an acute hæmorrhagic type with hæmaturia and much albumin and many epithelial casts in the urine.

Pathology.—In the great majority of cases of malaria the kidneys show little or no change. Occasionally, however, there is a massing of infected red cells in the renal capillaries accompanied by congestion, pigmentation, hæmorrhages and swelling and degeneration of the epithelium of the convoluted tubules.

(11) THE RESPIRATORY SYSTEM.

Symptoms referable to the respiratory system are not common in malaria, but in severe cases there may be considerable dyspnœa and the symptoms and signs of a mild bronchitis may be present. Especially in cases in which a relapse has been brought on by conditions of exposure and hardship the disease is liable to be complicated by true pneumonia. (See also Section III, p. 158.)

(12) THE SKIN.

Persons who have suffered repeatedly from malaria usually have a pale sallow complexion with a tendency to patches of pigmentation. Herpes of the lips is a common incident of the febrile attack and some patients suffer severely from urticaria. In chronic cases œdematous areas on the shins and feet may be detected. The fingers and toes of most persons who have suffered much from malaria are constantly "blue with cold," and this condition, when aggravated by unusually cold weather, may lead to the production of Raynaud's disease.

(13) THE MUSCULAR SYSTEM.

Patients who contract a simple infection during years of ordinary incidence may pass through many paroxysms without suffering much loss of weight or strength, and cases are recorded in which patients who have had a paroxysm of benign tertian fever every other day for a month have actually gained weight during the period. In tropical countries, where the disease is endemic, the indigenous inhabitants, although stunted in growth and intellectually dull as a result of the continued infection, are seldom emaciated, and in this respect the usual form of the disease differs essentially from the dangerous disease named *kala-azar* in which a similar enlargement of the spleen is always accompanied by great loss of flesh.

In the severe infections which occur during years of epidemic intensity muscular weakness and wasting is marked, and recovery from them may not be complete during the intervals between the frequent relapses.

(14) THE SUPRARENAL GLANDS.

A syndrome occasionally met with in pernicious attacks of malignant tertian fever and characterized by great muscular weakness; a constant low blood-pressure without change in the heart's action; pains in the lumbar region; headache; diarrhœa; vomiting; delirium; coma and death, has been attributed by Paisseau and Lemaire to acute changes in the suprarenal glands with adrenal insufficiency; but Dudgeon and Clarke, who in thirty-five cases combined a complete examination of the adrenals with an examination of the heart muscles and cerebral and other tissues, doubt if it would be correct to attribute the syndrome to a disturbance of the adrenals alone.

Pathology—In intense malignant tertian infections the most constant lesion in the suprarenal glands, according to Dudgeon and Clarke, is a reduction of the fatty lipoids of the cortical layers. The chromaffin content in the cells of the medulla was diminished. In five of the thirty-five cases thrombosis of capillaries with hæmorrhages into the gland and degenerative changes in the cortex with and without blocking of the blood-vessels were also present. In these five cases there was also a massing of parasites in the capillaries of the brain, and this, in all probability, was the pathological basis of the symptoms, at least as regards those referable to the nervous system.

CHAPTER VII (*continued*).

SECTION III.

(1) On Deaths from Malaria.

Unfortunately there are a good many exceptions to the general rule stated in Section I that the tendency of malaria which has been contracted during years or circumstances of normal endemic incidence is toward recovery. As a result of these exceptions, it happens that even the ordinary endemic form of the disease causes in the aggregate a large number of deaths every year, especially in localities where quinine is not readily available. It is estimated that in India in an ordinary year, and taking the country as a whole, the mean death-rate from malaria is about 5 per 1,000 of the population. This means about 1,130,000 deaths directly due to endemic malaria, and, as in such a year the disease is not very fatal, the number may be regarded as representing an enormous amount of suffering and loss of labour, often at a time when labour is of most value. We do not know the corresponding number of cases of malaria which occurred, nor do we know what proportion (if any) of fatal cases received quinine treatment. What we do know is that this ordinary form of malaria, when properly treated by quinine, is by no means a fatal disease, at any rate among adults. In India, a large number of the cases of malaria among European and native soldiers are so mild that it is often considered sufficient to treat them in their quarters instead of admitting them to hospital. Among European troops during the years 1906 and 1907, not many fewer than 10,000 cases of malaria were so treated. As regards cases which were sufficiently severe to require admission to hospital, the following statistics may be mentioned:—

Years	Class of patients	Number of cases treated in hospital	Number of deaths	Case mortality
1903-1907	European soldiers	63,597	99	0·16 per cent., or 1 death in 642 cases.
	Native soldiers	144,728	612	0·42 per cent., or 1 death in 236 cases.
	Native prisoners	189,534	681	0·36 per cent., or 1 death in 278 cases.
1898-1907	Wives of European soldiers ..	3,042	37	1·0 per cent.
	Children of European soldiers	5,128	86	1·68 per cent.

It has been surmised that in ordinary years in India, if we could place the native population in fairly good hygienic conditions, give them prophylactic doses of quinine during the fever season, and provide them with suitable food and adequate quinine treatment when attacked, we might prevent three-fourths of the deaths from malaria which now occur.

Turning now to the mortality caused by EPIDEMIC MALARIA, we find that the story is much more serious. The fatality experience of malaria in the recent war was chiefly in connection with this form of the disease, and on a smaller scale, under peace conditions, European troops in India in 1908 had a similar experience. In that year a devastating epidemic appeared in India about the end of September, and involved nearly the whole of the Punjab.

Major Christophers[1] reported that in areas most severely affected it prostrated almost the entire population, both native and European. The ordinary business of large cities was interrupted, no labour could be obtained, transport was disorganized, and even food-vendors ceased to carry on their trade. There was an alarming prevalence of pernicious cases and an almost unprecedented rise in mortality, the deaths being due in most cases not to protracted sickness, but to the intensity of the infection. In areas where the average non-epidemic mortality in October was usually between 100 and 125, the deaths in October, 1908, were between 1,500 and 2,300, and in the area comprising localities with seven times the non-epidemic death-rate, the deaths in that month, instead of numbering 6,841, were 76,256. Tracts affected by malaria to this degree were termed by Major Christophers "fulminant areas." When the epidemic was over, the inhabitants of localities which had been severely visited showed profoundly the effects of the disease. For some time there was a remarkable condition of almost universal infection with malaria, as evidenced by the presence of parasites in the blood, a high degree of splenic enlargement (the spleens being notably larger and more tumid than in non-epidemic years) and frequently recurring relapses. The effects of the epidemic on both European and native troops were very severe. Pernicious attacks of a fatal character were frequent, and, of the soldiers who survived, a large number presented for a long time a condition of intense anæmia, emaciation, and prostration, which was rightly termed "acute malarial cachexia." It was a common observation that the large doses of quinine which European soldiers were receiving once or twice a week as a prophylactic failed to prevent the frequent and almost regular recurrence of severe relapses, and that the doses seemed to have the effect of causing the appearance of numerous sexual forms of the parasite in the peripheral blood. Then, as in the recent war, many medical officers reported that their previous faith in the prophylactic value of quinine had been severely shaken. The after-history of many patients was similar to that of some of the unusual cases of malaria which we have seen recently.

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[1] "Malaria in the Punjab" (Government of India Scientific Memoirs, New Series, No. 46).

In the notable report already referred to, Major Christophers adds greatly to our knowledge of the mechanism of serious malaria of the type just described and of the more usual endemic type. From his account we realize how unlikely it is that any two or three cases of malaria should be of the same severity or fatality, or should relapse with equal frequency or rarity, or should be modified or cured by the same doses of quinine. It would seem, indeed, that it happens more or less by chance (perhaps in consequence of the annual recurrence of a series of quite similar circumstances acting upon a stable population) that the usual endemic disease gives rise to groups of cases of the same general severity and fatality, but that a study of the epidemic disease gives a truer idea of malaria as a morbid process in which each case must be regarded as a distinct entity corresponding to a particular infection which, in dose and virulence, is different from every other. This view helps us to understand why malaria is spoken of as "a protean disease," and indicates that it is less important to know the usual fatality-rate of the disease than it is to obtain all possible information of the source and character of infection in the particular case which is under our care.

Deaths from Malaria in England.—A study of the available records of true indigenous malaria in England shows, I think, that until the price of quinine fell sufficiently to bring the drug within the reach of the poor, even the endemic malaria of this country was quite frequently fatal. It shows, also, that occasionally there were "epidemic years" in which the disease caused a much higher mortality than usual. Dr. Stevenson, the Registrar-General, has made the interesting observation that the mortality statistics of "ague" in England seem to prove the existence of endemic foci of fatal malaria in Kent and the Fen country even up to comparatively recent times (1870 to 1880). These are the chief areas in which true indigenous cases of the disease can still be found. He has also noted that about 1880 an interesting change in the statistics began to occur. Prior to the beginning of the decade 1881-1890 the recorded deaths from ague among males and females were about equal: thereafter the deaths of females began to fall much more rapidly than those of males, as is shown in the marginal statement. At the close of the later decennial period dealt with in this statement, the total deaths were only a small

	M.	F.		M.	F.
1881	181	181	1901	88	10
1882	183	162	1902	99	13
1883	137	151	1903	60	9
1884	165	111	1904	95	11
1885	128	99	1905	71	8
1886	117	98	1906	55	15
1887	116	77	1907	62	6
1888	91	68	1908	49	7
1889	92	66	1909	69	11
1890	88	58	1910	44	7

fraction of the number in the earlier period, and there were from five to ten times as many deaths of males as of females registered. The assumed explanation is that in the earlier period the statistics included fatal cases of indigenous origin which naturally affected both sexes equally, but that by the beginning of the present century fatal cases of indigenous origin had almost ceased to occur, and the only cases which proved fatal were imported cases which were almost entirely in males. The more general use of quinine is not, of course, the only available explanation of the disappearance of the fatal form of indigenous malaria from the English statistics, but the reader has only to turn back to the records of the cases of R. B. and J. A., given on pp. 112-113, to realize that even at the present time some of the cases which originate in the country might prove fatal if the nature of the illness were not discovered and adequate quinine treatment applied.

This point has also a very important bearing in connection with cases of malaria in England among soldiers, sailors, and civilians, whose infection has been contracted abroad. During recent years the number of deaths in this country registered as due to malaria contracted abroad has been usually between 50 and 60 per annum, but in 1917 the number rose to 126, in 1918 to 197, and in 1919, if the rate of mortality prevailing during the first six months continued throughout the year, the number would be 280. The following figures have been kindly supplied to me by Dr. Stevenson, Registrar-General.

DEATHS FROM MALARIA IN ENGLAND BY YEARS AND AGE GROUPS.

	Deaths occurring in England from malaria			Age groups of deaths from malaria during the first six months of 1919	
	Males	Females	Total	Age groups	Number of deaths
1910	44	7	51	Up to 15	1
1911	56	2	58	,, 20	32
1912	49	9	58	,, 25	35
1913	49	9	58	,, 30	19
1914	56	4	60	,, 35	19
1915	55	10	65	,, 40	16
1916	59	3	62	,, 45	8
1917	122	4	126	,, 50	2
1918	188	9	197	,, 55	1
First 9 months of 1919	196	8	—	,, 60	2
				Over 60	4
					139

It will be seen that a disquieting feature of the deaths in 1919 (and the same was true of the deaths in 1918) is that most of them were of young men.

It is a sad truth that in at least some instances death might have been prevented if there had been early recognition and adequate quinine treatment. This matter is of such importance that I make no apology for emphasising it by recording two examples as follows:—

(1) A soldier who had suffered from malaria in Egypt came home on leave to a populous district in England on July 22. On the 24th he had a slight febrile attack but got up the next morning. On the 29th he had to go to bed again with fever and great aching in the bones, but it was said that he had no definite rigor or sweating. A doctor who was called in diagnosed influenza and prescribed a mixture containing sodium salicylate. On August 2 the temperature was still high and there was much vomiting. The salicylate mixture was repeated. On the 4th the eyes were jaundiced and the liver somewhat enlarged. Malaria was then suspected for the first time and a mixture containing 2½ grains of quinine to the dose was prescribed to be taken every four hours; but on account of the continuous vomiting it was doubtful if much could be retained. On the 7th the patient seemed better, but next day he was sullen, drowsy and delirious, and passed porter coloured urine. On the 9th both parotid glands became enlarged; on the 10th there was no fever, but jaundice had increased and the patient was only partly conscious; on the 11th he had a profuse sweating attack, and died a few hours later. An examination of a film of peripheral blood taken after death showed numerous crescents and ring forms of the malignant tertian parasite.

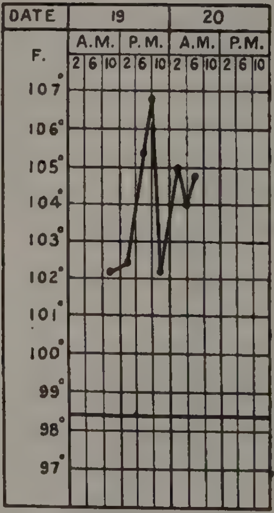

Fig. 85.—Chart of H. C.

(2) A cargo steamship left Bathurst (West Coast of Africa) on January 5 on her return voyage to England. She carried no doctor. She had been "up the creeks" about sixteen days and mosquitoes had been very troublesome. On January 16 the chief officer died. He had been ill for six or seven days but malaria was not suspected, and no quinine had been taken. On the day of his death an apprentice, H. C., complained of being ill, but his temperature was normal. The next day (the 17th) his temperature was 100° F. and as he appeared to show signs of malaria he was given quinine according to the directions in the "Ship Captain's Medical Guide." The ship was now in the English Channel, so the master altered course to proceed to the nearest port in order to obtain medical assistance. Owing to fog a suitable port was not reached until 6 a.m. on the 19th. A doctor came on board at once and took the patient to a hospital on shore. At this time the patient was in a semi-comatose condition. It was found at the hospital that he had high fever, and was markedly jaundiced. It was thought that the case might be one of yellow fever, but apparently

malaria was not suspected, and no quinine treatment was given. The patient's temperature rose as shown on the accompanying chart (fig. 85) and he died next morning.

At an examination made after death numerous malignant tertian malaria parasites were found in the blood and splenic tissue.

(2) ON MALARIA IN CHILDREN.

In malarious places in the Tropics native children who have greatly enlarged spleens and many parasites in their blood often seem to be very little affected by the disease. From this common observation it has sometimes been inferred that children suffer less severely from malaria than adults. As a general rule this is never true. In these highly endemic localities the malarious children who appear, on superficial examination, to be healthy, are those who, after much chronic ill-health, have succeeded in surviving repeated attacks until a tolerance to the effects of the parasitic invasion has been acquired. And it will always be found that in places where children above 10 years of age show this tolerance, the death-rate among infants and others under 5 or 6 years of age is very high. It has been observed in India that the death-rate of children in areas of high malarial endemicity is twice as high as in non-malarious areas, and that such areas can be mapped out on the basis of the total mortality of children between 2 and 5 years of age. Major Kenrick, who studied this subject in the Central Provinces of India, noted that, while deaths from malaria in adult natives are due usually to complication with some added disease, children are killed by the intensity of the parasitic invasion. He recorded the following as being a frequent history of fatal cases of uncomplicated malaria in native children:—An apparently healthy child has an attack of fever lasting seven or eight days. The child then appears to be quite well for two or three weeks, when there is another bout of fever which is followed by another apyrexial period. The relapses now begin to occur at more frequent intervals and with greater severity. In the absence of quinine, unless the child succeeds in surviving until it has acquired a certain degree of immunity, death occurs often with cerebral symptoms. In one such case a well-nourished child had been unconscious with high temperature and convulsions for four days when first seen. Blood examination showed a mixed infection with quartan parasites and crescents.

In Macedonia, according to Armand Delille, the symptoms of malignant tertian malaria in children are often atypical and cannot be diagnosed without blood examinations. The primary illness commences insidiously with gastric trouble, fever, and either marked drowsiness and somnolence or insomnia and restlessness. There is anorexia, but great thirst, so that a breast-fed child starts feeding frequently, but abandons it in a few moments. The tongue is dirty and coated, the stomach distended, and there may be vomiting. In breast-fed infants dysenteriform diarrhœa occurs, but older children are usually constipated. Anæmia progresses rapidly, the face becoming pale and drawn and with dark rings under the eyes. There is usually no abnormality in the heart or lungs. The temperature varies between 102° and 103° F., showing as a rule very short periods of remission or intermission, so that unless the temperature is recorded at frequent intervals the chart may show almost continuous fever. The spleen quickly enlarges until it is two or three fingers' breadth below the costal margin. Death may result from an acute primary cachexia, but many cases of moderate intensity survive the primary attack and pass into a condition of chronic splenomegaly.

Among the civilians who contracted malaria in England between 1917 and 1919 no fewer than 75 per cent. were children. These cases have afforded an opportunity of studying primary attacks of benign tertian malaria among children in this country. In the great majority the manifestations have been quite typical, but more severe than in most of the indigenous cases among adults. In some cases an irregular temperature and absence of characteristic attacks of shivering and sweating caused delay in diagnosis, and in a few the symptoms were so mild that the illness was not observed by the parents, but was discovered during special inspections of school children. A brief description, with temperature charts, of two of the less typical cases, has already been recorded on p. 112. The case of R—— B—— is noteworthy for the considerable enlargement of the liver, the tendency to bleeding, the absence of definite chills and sweating, and the severe anæmia. The other case, C—— A——, was thought at first to be due to a septic condition of the mouth. The fever after admission to hospital was irregularly remittent, partly as a result of insufficient doses of quinine. The following case illustrates the usual type of the disease and the great splenic enlargement which is a feature of many cases in children. J. A., aged 8 years, living on a farm in Essex: The case was diagnosed as malaria by a local medical practitioner, who had observed that the child was suffering from daily febrile paroxysms, the temperature rising to 102° F., and accompanied by severe sweating but no rigor. On admission to hospital on August 25, a blood-film was taken and found to contain many benign tertian parasites. The patient was markedly pale and had *herpes labialis*. Tongue dry but clean. Pulse regular, of moderate volume and tension. Heart sounds clear; the apex beat in the fourth space in mid-clavicular line; area of dullness normal. Lungs, no abnormality detected. Spleen greatly enlarged, extending in the mid-axillary line from the seventh rib to the level of the umbilicus and in the horizontal direction touching the umbilicus. Liver, no definite enlargement detected.

The patient was at once put on quinine, three grains three times a day. The temperature chart is reproduced below (fig 86).

Recovery was continuous but slow. On September 17 there was a relapse, with a rise of temperature to 102° F., but no parasites could be found in the peripheral blood. The patient was discharged from hospital, temporarily cured, on October 4.

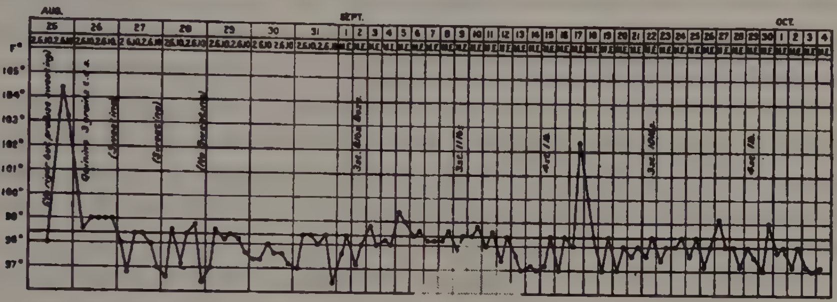

Fig. 86.—Chart of J. A. The chart shows a relapse in which no parasites were found.

Mention of the relapses which occur in true indigenous cases has already been made on p. 92. The following is an example of the occurrence of relapses in a child The case also illustrates the remarks on p. 111 in connection with the failure to find parasites during a mild primary attack.

Stanley H., aged 8. First attack September 13, 1919. The notification stated that he suffered from an attack of shivering every other day. No parasites were found in the blood films sent for diagnosis, but the attacks yielded readily to quinine. The case was notified again on January 20, 1920 (which was four months since the primary attack) for a relapse which began on the 18th. On this occasion benign tertian parasites were numerous in the peripheral blood. Within a few days the relapse was cured and the parasites disappeared. Exactly a month later (February 18, 1920) there was a second relapse, again with many parasites in the peripheral blood.

(3) On Pernicious Symptoms.

The term "pernicious" is best used for the clinical purpose of indicating any symptom or sign which, in the course of an acute malarial attack, appears to threaten life. The symptom may be dangerous either directly from its severe character (e.g., hyperpyrexia), or indirectly by interfering with satisfactory treatment (e.g. persistent vomiting).

Pernicious symptoms are rare in cases contracted during seasons of ordinary endemic prevalence, but are quite frequent in the epidemic type of the disease They may arise in infections with any of the species of parasite, but are more common in infections with the malignant tertian species (*P. falciparum*) which for this reason is sometimes called "the pernicious parasite."

The fatal cases of malaria described above are good examples of cases with marked pernicious symptoms. They serve to emphasize again the statement made on p. 112, that in any acute illness in a person who has been to a malarious country we should keep the possibility of malaria constantly in mind. It is characteristic of many pernicious symptoms that they tend to prevent the prompt diagnosis of the disease. They may do so either by presenting in a prominent manner a symptom which suggests strongly some other condition than malaria, such as sunstroke, alcoholism, apoplexy, acute heart failure, dysentery, cholera, appendicitis, &c.; or by presenting, in a patient who is obviously very ill, an almost complete absence of what are known to be the usual clinical signs of malaria. Cases in which the patient appears to be overwhelmed as if by an acute toxæmia are of this nature.

The following is a list of pernicious symptoms, one or more of which may be met with in different cases :—

I.—SYMPTOMS NOT REFERABLE TO A PARTICULAR SYSTEM.

(1) Fever of a typhoid-like type; (2) bilious remittent fever; (3) hyperpyrexia; (4) toxæmic symptoms of an algide type; (5) uncontrollable sweating and collapse; (6) hæmorrhagic symptoms; (7) hæmoglobinuria; (8) acute progressive anæmia.

II.—SYMPTOMS REFERABLE TO LOCALIZATION OF THE EFFECTS OF THE INFECTION IN PARTICULAR SYSTEMS.

(i) *The Nervous System:* (1) Intense headache; (2) irritability and restlessness; (3) delirium; (4) convulsions; (5) epileptiform seizures; (6) unconsciousness; (7) coma; (8) meningitic symptoms; (9) hemiplegia and paraplegia; (10) localized paralyses (facial, &c.) and neuritis; (11) tremors and ataxy; (12) changes in speech and aphasia; (13) mental changes and definite malarial psychoses.

(ii) *The Digestive System and Abdominal Viscera:* (1) Severe epigastric pain; (2) severe splenic pain; (3) simple or bilious persistent vomiting; (4) hæmatemesis; (5) choleraic diarrhœa: (6) dysenteric diarrhœa; (7) melæna; (8) pronounced jaundice; (9) symptoms simulating acute appendicitis or acute peritonitis; (10) rupture of the spleen.

(iii) *The Circulatory System:* (1) Fainting attacks; (2) sudden heart failure; (3) very low arterial tension; (4) symptoms of thrombosis and small vascular hæmorrhages.

(iv) *The Respiratory System:* (1) Dyspnœa; (2) symptoms simulating acute bronchitis or pneumonia; (3) acute failure of respiration (affection of respiratory centre).

(v) *The Urinary System:* (1) Albuminuria; (2) nephritis; (3) incontinence or suppression of urine; (4) uræmia; (5) hæmaturia; (6) hæmoglobinuria.

(vi) *Other Systems:* (1) Purpura; (2) œdema; (3) gangrene of extremities; (4) affections of hearing, speech, sight, taste; (5) orchitis, parotitis, mastitis, and other glandular affections.

Many of these symptoms arise not in the beginning of an acute pernicious attack but as a later manifestation in cases which, from failure of diagnosis, have remained untreated with quinine for several days.

In order of frequency the commonest cases with pernicious symptoms are those without predominant local manifestations in one system rather than in another. The patient when first seen presents a "typhoidal" condition with moderately high fever which appears (unless the temperature is taken very frequently) to be practically continuous or only slightly remittent. The abdomen is usually tender on palpation and it may be difficult to ascertain whether the spleen is enlarged. The patient is drowsy and perhaps slightly delirious but may answer questions rationally. The heart and lungs appear to be normal and it may not appear that the patient is markedly anæmic. In the absence of microscopic examination of the blood the diagnosis remains in doubt, and, if "expectant treatment" is adopted, the patient may gradually sink without any definite localization of symptoms. It is especially in this class of case that immediate microscopic examination of the blood has often been the means of saving life. When called to a case of this kind we must banish from our minds the knowledge that malaria is *usually* a disease with definite paroxysms of rigor, heat, and sweating; we must waste no time upon detailed clinical examination or inquiry into history; we must at once proceed to the essential diagnostic method of microscopic examination of the blood. This should be done *very carefully and thoroughly*, if possible in the patient's house, and in any case without a moment's unavoidable delay. The discovery of parasites or other unequivocal evidence of malaria must be followed at once by the administration of quinine intravenously. The whole procedure of both diagnosis and treatment need not, as a rule, occupy more than forty minutes. Promptly to carry this procedure to a successful issue with its consequent saving of life, is one of the most satisfying, as it is one of the most helpful, experiences which can fall to the lot of a physician.

For a description of the various pernicious symptoms enumerated above it will be more profitable, I think, to give extracts from notes on actual cases than to deal with the subject in a general way.

EXAMPLES UNDER HEADING I, SUB-HEADINGS (2), (3), (6), (8).

A native soldier was admitted into hospital on October 13, 1907, complaining of intense headache, giddiness and fever. Temperature 102° F. He had vomited three times, the vomit being bilious in character. The temperature fell to subnormal with very profuse perspiration. The next day he began to have bilious diarrhœa as well as vomiting, and in the evening he became unconscious. For the next three days the patient was conscious in the morning, but unconscious in the evening, when the temperature rose to 102° or 103° F. The vomiting ceased, but bilious diarrhœa continued. On the seventh morning of his illness he had low muttering delirium with twitching and jerking of the limbs, and his pulse became thready and intermittent. He gradually fell into a state of coma and died. Malignant tertian parasites were found post mortem. (*Bilious type with cerebral symptoms.*)

A native soldier was under treatment in hospital for an ordinary attack of ague. He progressed favourably for some days when the temperature suddenly rose one evening to 105° F. Quinine was injected intramuscularly, but two hours afterwards the temperature had risen to 107·4° F. Cold sponging brought it down to 105° F. Next day the temperature was normal, and it remained so, but severe diarrhœa set in, and the patient died. (*Hyperpyrexia and diarrhœa.*)

A European soldier was admitted into hospital at Ferozepore (India) on November 26, 1907, suffering from malignant tertian fever of an irregular type and jaundice. He had severe epigastric pain, bilious vomiting (the vomit containing blood), loose hæmorrhagic stools and port wine coloured urine. Later he had severe lumbar pains and an attack of hæmaturia. He got better, but had a sudden attack of dyspnœa and died. (*Hæmorrhagic type.*)

A native soldier was admitted on August 29, 1907, with a temperature of 101° F. He was drowsy and complained of much pain in the splenic region. He passed two hæmorrhagic stools during the night. Next day he was only semi-conscious. He vomited several times, the vomit containing blood, and passed a number of hæmorrhagic stools. On the 31st he was quite unconscious, and both legs and the left arm were rigid. He died the same day. (*Hæmorrhagic type.*)

A native soldier was admitted into hospital at Mauritius on March 9, 1906, with fever and a palpable spleen. He had typical attacks of ague daily, the chart being of the double tertian type. Quinine was given hypodermically, but it had little or no effect on the fever. On the 21st he had some œdema of the ankles and feet, and his urine contained albumin. Quinine in various forms was tried, but he continued to become more and more anæmic, and low fever continued. On April 10, he was profoundly anæmic and extremely weak, and had some paralysis of the legs. A few days afterwards he died from heart failure. (*Type of malignant fever with acute progressive anæmia.*)

EXAMPLES UNDER HEADING II.

(1) *Symptoms chiefly in the Nervous System.*

A European soldier was admitted into hospital on the evening of November 9, 1907, with a temperature of 103° F. He complained of intense headache. The next morning his temperature was subnormal. The spleen was palpable and tender. A blood examination showed the presence of numerous malignant tertian ring parasites. At 10 p.m. the same evening his temperature rose to 105° F., and he became unconscious. Shortly afterwards he became comatose, fæces and urine being passed involuntarily. The coma became more profound and ended in death. (*Cerebral type with coma.*)

A native soldier suddenly became ill while on parade. He was taken to hospital, and his temperature was found to be 106° F. Severe vomiting set in, and after profuse sweating the temperature fell to 103° F. Malignant tertian parasites were found in his blood. Quinine was given per rectum. By sponging, &c., the temperature was reduced to 100·6° F., but low muttering delirium began. Next day the temperature was 104° F. The delirium persisted, and he became very violent. He died suddenly from heart failure. (*Cerebral type with hyperpyrexia, delirium, and heart failure.*)

A European soldier was admitted into hospital with malignant tertian fever. The next day he had an epileptiform attack followed by semi-coma associated with choreiform movements of the arms and legs. He recovered. (*Cerebral type with epileptiform seizure.*)

An officer who had had fever in Damascus was admitted to hospital in an anæmic condition and with slight evening fever. He was given 30 grains quinine daily for ten days and discharged on November 22 to a convalescent institution. On the 24th he had a malarial attack with transient left hemiplegia which cleared up in two hours; readmitted to hospital. November 25, a "faint"; November 27, a Jacksonian fit; he recovered at once; a similar attack later and he remained unconscious the rest of the day, but complete left hemiplegia and hemianæsthesia could be demonstrated. Given quinine intramuscularly. November 28 still unconscious, but power had returned on the left side; no reflex change. Quinine repeated. November 29, irrational. November 30, fairly rational. December 1, quite clear but a little "childish." (*Hemiplegia and mental changes.*)[1]

A native soldier was under treatment in hospital suffering from intermittent malarial fever, the temperature ranging between subnormal and 104° to 105° F. He had intense headache and diarrhœa, the motions being grass green in colour. Cerebral symptoms set in with the occurrence daily of an epileptiform convulsion which lasted for some minutes. Malignant tertian parasites were found in his blood. Quinine was given hypodermically, but the disease was fatal. (*Cerebral type with diarrhœa and epileptiform attacks.*)

(2) *Symptoms chiefly in the Digestive System.*

A native soldier was brought into hospital in a collapsed condition, and with a subnormal temperature. He had persistent vomiting and profuse diarrhœa, the stools being watery, with small white flakes (cholera like). Nothing resembling the cholera vibrio was found on microscopic examination of the fæces, but when the blood was examined, numerous crescents were immediately found. Quinine in doses of 10 grains was given hypodermically, and the next day the patient's condition was much improved. On the second day after admission the vomiting and diarrhœa stopped. (*Choleraic type.*)

A European soldier was admitted complaining of dysentery. He had ten loose motions containing pure blood mixed with black blood and mucus during the day. There was no fever. Numerous crescents were found in a film of peripheral blood. Quinine was injected intramuscularly, and he quickly recovered. (*Dysenteric type.*)

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[1] Recorded by Dr. Carmalt Jones in the *Lancet*, December 20, 1919, p. 1133.

A native soldier was admitted complaining of attacks of diarrhœa, which had come on regularly every week, or ten days, for a month. The motions were grass green in colour. His temperature was 102·4° F. Many malignant tertian rings and crescents were found in his blood. The fever and diarrhœa yielded readily to quinine given intramuscularly. (*Diarrhœic type.*)

Pte. H. Three attacks of benign tertian malaria, said always to have begun with vomiting. While under observation there was an uncontrollable attack of vomiting of two hours' duration, and ending in grave collapse. (*Persistent vomiting.*)[1]

Corporal F., age 32, admitted to hospital on September 20, 1916, in Salonika, with profuse diarrhœa and pyrexia. The bowels were moving about every hour. The stools were fluid, fæculent, heavily tinged with bile and blood. The spleen was enlarged and hard, and a blood-film showed a very heavy infection with subtertian parasites of all types, rings, rosettes, and crescents. He was treated with intravenous quinine and salines. Examination of the stools for dysenteric organisms and protozoa was negative. The diarrhœa continued, the stools constantly containing blood and traces of mucus. Ultimately the patient became incontinent, and died eight days after admission. (*Severe dysenteric type*).[2]

A European soldier complained of colicky pains in the abdomen and fainting fits. He was extremely anæmic, and in a condition of collapse. Benign tertian parasites were found in his blood. There were abdominal distension and suppression of urine. Uræmic symptoms developed, and he died in a state of coma. At the post-mortem examination it was found that the spleen had ruptured. (*Spontaneous rupture of the spleen.*)

(3) *Symptoms chiefly in the Circulatory System.*

A native soldier was admitted into hospital on September 13, 1907, with a temperature of 103° F. Benign tertian parasites were found in his blood. He progressed favourably until the 22nd, when signs of heart weakness developed. On the morning of the 23rd he had a sudden syncopal attack, and died. (*Syncopal type.*)

Driver J. (Macedonia), age 39. On admission too ill to give a history. Is pallid, cachectic, with slight icterus; tongue very dry and brown, crust of old herpes on lips. Temperature 100° F. Pulse feeble. Lungs *nil*; urine *nil*; spleen enlarged. Blood film: very scanty rings present. Heart: no enlargement of cardiac dullness. No bruits, but the sounds muffled, short, and toneless—"reminiscent of what is heard in diphtheria." Instructions were given that the patient was to be kept lying absolutely flat, not even to raise his head. On the afternoon of admission the patient had a syncopal attack lasting nearly half an hour, during which the pulse became rapid, and almost imperceptible. Next day he had several attacks of heart failure, and died at 7 p.m. He was quite conscious throughout. After death diffuse fatty change was found throughout the cardiac muscle, and parasites were present in the brain. (*Syncope associated with fatty degeneration of the heart.*)[3]

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[1] Recorded by Dr. Carmalt Jones in the *Lancet*, December 20, 1919, p. 1,133.

[2] Recorded by Major Falconer and Captain Anderson in the *Journal of the Royal Army Medical Corps*, February, 1918, p. 215.

[3] Recorded by Dudgeon and Clarke in the *Quarterly Journal of Medicine*, vol. xii, No. 48, July, 1918.

(4) *Symptoms chiefly in the Respiratory System.*

In a paper already quoted Major Falconer and Captain Anderson record in detail two cases of malaria in which well-defined chest signs and symptoms suggested lobular consolidation of the lungs, but in which the temperature charts were characteristic, not of lobular pneumonia, but of a malarial attack. In both cases malignant tertian parasites were found in the blood, and the condition cleared up under quinine treatment. Dudgeon and Clarke have shown that, in pernicious attacks of malaria, scattered areas of consolidation of lung tissue may occur as a result of congestion of capillary vessels and hæmorrhages into the alveoli.

The following fatal case recently occurred in England :—

A soldier who had contracted malaria in East Africa continued to suffer from relapses after returning to England. On February 1 he had a severe rigor with a rise of temperature to 103° F. During the next five days the temperature varied between 102° and 104° F. On the sixth day it fell to 100° F. and the patient felt much better and sat up in bed for some time. Next day he complained of severe pain in the side "like pleurisy." His temperature rose to 103° F., there was marked dyspnœa and he became delirious. Physical signs of pleuro-pneumonia developed rapidly, and he died two days later.

(5) *Symptoms chiefly in the Urinary System.*

A case with hæmaturia has been mentioned above.

Dudgeon and Clarke[1] record the following case :—

Private M. had malaria in April, 1917. No history of previous illness. On November 22 he had swelling of legs and feet, dyspnœa, vomiting, and cough. The urine contained albumin. On the 26th there was slight œdema of the eyelids, feet, and hands, and a blood film contained crescents. He died on this day after five uræmic fits. At the post-mortem examination acute tubal nephritis with extreme tubal degeneration was found. (*Nephritis and uræmia.*)

(6) *Other Systems.*

A native soldier was admitted into hospital at Mauritius on September 21, 1906, suffering from fever. Quartan parasites were found in his blood. Thirty grains of quinine were given daily for a week but he developed great œdema of the legs and intense anæmia. Ultimately he recovered. (*Primary cachexia with œdema.*)

A European soldier was admitted to hospital in Salonika on October 27, 1916, with marked œdema of the legs, the subcutaneous tissues of the back, the abdomen and the face. Signs of fluid in the abdominal cavity were present. The spleen was enlarged to the umbilicus and the liver was half an inch below the costal margin. There was no evidence of disease in the heart or lungs and the urine contained no albumin or casts. Malignant tertain crescents and rings were found in the blood. Under energetic quinine treatment the œdema of the extremities and the physical signs of ascites had completely disappeared fifteen days after admission. (*Acute primary cachexia with general œdema and ascites.*)

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[1] See previous reference.

A European soldier, aged 26, was admitted to hospital in Salonika on October 4, complaining of loss of use of his legs and numbness of the feet. His temperature was 102° F., the conjunctivæ were slightly icteric, and the spleen palpable. A blood film contained numerous malignant tertian parasites. Both feet were œdematous and there was a large purple ecchymosis on the dorsum of each foot. Most of the toes were swollen and almost black and there was a purple patch on the soles of both feet. Under appropriate antimalarial treatment the fever and parasites disappeared and the condition of the feet rapidly improved. Except for some superficial necrosis on the dorsum of the right foot no after-effects were left. (*Gangrene of the feet.*)[1]

(7) *Blackwater or Hæmoglobinuric Fever.*

[*Note.*—For convenience, the diagnosis, treatment and prevention, as well as the symptomatology, of this affection are included here.]

Certain susceptible persons who have suffered repeatedly from severe malaria are liable to be attacked with the dreaded disease called blackwater fever. The disease consists essentially in the occurence of one or more paroxysms of hæmolysis of red corpuscles in the blood stream with consequent hæmoglobinuria.

Since the war an appreciable number of cases have occurred in England among malarious soldiers after their return from the Balkans and other Eastern fronts. The following is an example of such a case:—

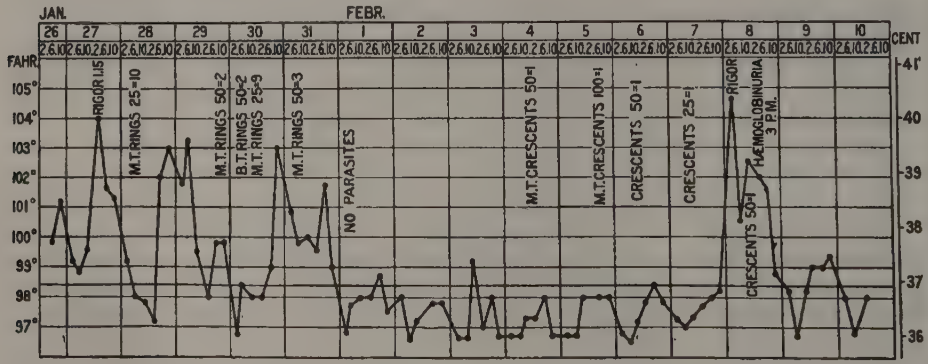

Fig. 87.—Chart of a Case of Blackwater Fever.

Pte. T., had his first attack of malaria at Salonika in September, 1916. The type of infection was not stated. He remained in Salonika sixteen months, during which he had fourteen severe attacks. He became somewhat cachectic and was invalided home, arriving at a hospital in England on January 26, 1918. On admission he had some fever and his blood contained malignant tertian malaria parasites. The heart, lungs and urine were normal and the spleen not palpably enlarged. His temperature chart after admission is shown above (fig. 87).

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[1] Recorded by Major Falconer and Captain Anderson in the *Journal of the Royal Army Medical Corps*, February, 1918, p. 223.

At 2 a.m. on the 8th he had a severe rigor with rise of temperature to 104·8° F., and much nausea and vomiting. Some hours later he presented a peculiar ash-grey appearance with yellowness of the conjunctivæ, and his spleen was palpable and very tender. He complained of much dizziness and epigastric pain. At 3 p.m. he passed mahogany-coloured urine, which was found to contain hæmoglobin when examined with the spectroscope. It contained much albumin and left a heavy deposit on standing, but no red cells were found in it. Next day the urine was much lighter in colour but the skin and conjunctivæ were deeply jaundiced. The patient remained very weak for some time after the attack but made a good recovery.

Diagnosis.—The rule to inspect the urine frequently in all malarial attacks, both during and after the rigor, should never be neglected; for the discovery that a patient has passed "red-water" or "black-water" is often the first intimation of the nature of his illness. The urine may vary in colour from a light pink or light red to dark porter or nearly black. The presence of oxy-hæmoglobin (and in later stages met-hæmoglobin) must be confirmed by the use of the pocket spectroscope. If the case is not seen in an early stage it may be necessary to dilute the urine considerably before examining it with the spectroscope. The urine, when boiled, becomes almost solid from the presence of albumin, but usually no blood cells can be found on microscopic examination and it contains no bile pigment. When allowed to settle in a test-tube it presents a voluminous deposit, which, on microscopic examination, will be found to contain numerous granular casts.

Examination of the blood gives, as a rule, little or no assistance to diagnosis. In the general destruction of blood corpuscles which occurs during the blackwater fever process, corpuscles containing parasites are among the first to be dissolved, so that it is almost useless to attempt to find malaria parasites after the paroxysm has set in. The blood is usually thin and watery, the red cells may fall to two millions or less per cubic millimetre, and the hæmoglobin value to 25 or less per cent. of the normal.

Anuria, resulting from a mechanical blocking of the renal tubules by blood debris, is a complication in some severe cases, especially when more than one hæmoglobinuric paroxysm has occurred. When called to a case in which, for this reason, no urine is available, the following points may aid in diagnosing the disease: (1) a history that the patient is a malarial subject who has suffered from relapses "off and on" for some months; (2) after perhaps some premonitory symptoms (which may have followed unusual exposure or a chill), the onset of what the patient takes to be an exceptionally severe malarial rigor often accompanied by bilious vomiting, epigastric pain, and great prostration; (3) the rapid appearance of intense anæmia followed in a few hours by jaundiced eyes and skin; (4) an enlarged and tender spleen and sometimes an enlarged liver with marked pain on palpating the epigastrium.

The disease is easily differentiated from severe bilious remittent malarial fever, ictero-hæmorrhagic jaundice, acute yellow atrophy, and yellow fever, by the characteristic hæmoglobinuria which does not occur in those diseases.

Treatment.

The most important points are:—

(1) *Absolute rest in bed.*

(2) *The most skilled nursing available.*

(3) Immediate cessation of quinine treatment.

(4) The free administration of alkaline drinks, barley water, and saline enemata or injections.

(5) A continuous watchful endeavour to allay troublesome and dangerous symptoms.

The actual paroxysm cannot be cut short by any drug at present known, and it is probably better to rely upon very careful nursing and watchful attention to symptoms than on any of the drugs which have been recommended from time to time. In my opinion, even if malarial parasites can be found in the blood at the beginning of the attack, quinine should not be given. The blackwater fever process itself destroys most, if not all, the parasites which may be present in the peripheral blood, and there is a danger that a curative dose of quinine may bring on another hæmoglobinuric paroxysm. But, before deciding to withhold quinine, the practitioner must assure himself, by the use of a spectroscope, that he is really dealing with a case of blackwater fever, not with a case of severe bilious malaria with very dark urine. Some time ago I saw a case reported as blackwater fever. The patient had high fever, was markedly jaundiced, and the spleen and liver were enlarged. I was shown a small quantity of very dark urine. Spectroscopic examination of the urine showed no indication of the presence of hæmoglobin. A film of blood contained numerous malignant tertian parasites. Prompt treatment with quinine, at first intravenously, then by the mouth, quickly cured the patient.

The chief symptoms which may have to be combated during an acute attack of blackwater fever are vomiting, epigastric and lumbar pain, prostration, cardiac failure, and suppression of urine. It is important to watch the blood-pressure carefully, as it tends to fall rapidly with the decline in temperature which follows the rigor. In most cases the kidneys can be kept sufficiently flushed by getting the patient to drink as much soda water, barley water, tea, &c., as possible. In dangerous cases saline injections should be given intravenously with the usual strict precautions. Simple diaphoretics may be given, but no antifebrile drug which is likely to depress the heart. Digitalin may be given to combat cardiac failure, and a drink composed of one part of champagne to two parts of soda water is comforting to the patient and will help to stop vomiting and prevent prostration.

The great weakness and anæmia which result from an attack require careful nursing and treatment, and the patient's blood should be examined at frequent intervals for a fortnight or more after the attack to ascertain the presence or absence of malaria parasites and by means of the hæmoglobinometer and hæmacytometer.

Prevention.—Blackwater fever occurs only in persons who have suffered repeatedly from malarial attacks. Therefore to prevent it we must endeavour to prevent the recurrence of those attacks. With our present knowledge the best advice that we can give to a person who has had an attack of blackwater fever is: (1) that he should not reside in a locality where he will be liable to reinfection with malaria; (2) that he should live in as normal and regular a manner as possible, avoiding excesses and being careful not to subject himself to chills, wettings, &c.; (3) that he should have his blood examined at frequent intervals for the early detection of malaria parasites or other indication of a probable relapse; (4) that unless he has a special susceptibility to the drug he should take a dose of 10 grains of quinine daily for three months after his attack of blackwater. If he is very susceptible to the drug a dose of 5 grains daily will be sufficient. These prophylactic doses can be begun with safety a week after his recovery from the attack of blackwater fever, or earlier in the unlikely event of parasites being found in his blood within a day or two of his recovery; (5) if in spite of these precautions the patient gets a relapse of malaria, he should go to bed at once, and an endeavour should be made to cure the relapse as quickly as possible. If the patient will remain in bed under careful nursing this can almost always be effected by doses of 10 grains of quinine three times on the first and second days of the relapse. During this treatment the urine should be inspected frequently to ascertain any sign of the presence of hæmoglobin, in which event the quinine should be stopped at once.

(8) *On Other Complications and Sequelæ.*

Most of the symptoms and signs which may complicate the diagnosis or treatment of a case of malaria are included in the pernicious symptoms described above. Of those which remain to be mentioned the most important are due to coincident infections with other diseases such as typhoid or paratyphoid fever, yellow fever, pneumonia, influenza, cholera and dysentery. In malarious localities it is necessary always to be on the alert to detect signs of a malarial attack in patients who are suffering from any of the acute specific fevers. For example, typhus fever, relapsing fever, and Malta fever are, in rare instances, complicated by malaria, and it is by no means uncommon for a patient who is convalescing from typhoid fever to be prostrated by a relapse of a former malarial infection. The clinical term "typho-malarial fever" was coined by an American Army Surgeon to designate mixed infections with those two diseases. The name must not be used for cases of "malaria of a typhoidal type." Especially in Macedonia during the summer of 1916 many severe cases of malignant tertian infection began with symptoms and a febrile course very like typhoid fever.

Yellow fever and malaria are frequently coincident. At a quarantine hospital at Guayaquil in Ecuador I found malaria parasites in the blood of four out of eleven yellow fever patients. In one of these cases the temperature chart for three days was typical of benign tertian malaria; it then took on the characters of a yellow fever chart and the patient died from this disease. It is possible that failure to recognize the coincident occurrence of these two diseases has led to some erroneous clinical descriptions of yellow fever, on the basis of which its occurrence has occasionally been recorded in localities which are free from it.

Pneumonia is sometimes coincident with malaria; and bronchitis more frequently. During the recent influenza epidemic the occurrence of influenza in patients already suffering from malaria added greatly to the severity of their illness; and the fatality among such patients was high. Matko in Vienna reported thirty deaths among thirty-eight malaria patients attacked with influenza during the epidemic. Dr. W. H. Willcox and Major Mavor have recently given some details of an outbreak of malignant malaria in Northern Persia which was complicated by epidemic influenza. The attacks of malaria were obviously protracted and rendered more severe by the influenzal infection, and they failed to react to large doses of quinine given by the mouth. The following example is recorded by Major Mavor:—

> Sergeant M., malignant tertian and influenza. Paroxysms with temperature rising to 105° or 106° with remissions to about 101° F. Quinine in solution by the mouth for three days. Maniacal delirium; hæmolysis; jaundice. Quinine 10 grains intramuscularly given daily in addition to the oral doses. Range of fever now about 102° to 99° F. No delirium, but profound anæmia. Jaundice improved. Parasites still present. This persisted for twelve days without change. On the twelfth day quinine 7 grains was given intravenously and repeated next day. Temperature fell to normal on the evening of the thirteenth day and convalescence proceeded normally with only two mild relapses.

Failure to recognize the coincident occurrence of trench fever in a patient suffering from malaria has sometimes led to difficulties in diagnosis and treatment. The same remark applies to the occurrence of ankylostomiasis, amœbic dysentery, kala-azar, filariasis and various other diseases in malarious patients.

I have seen a convalescent from true cholera who, without apparent cause, suffered from fainting attacks, passing into a condition of collapse and unconsciousness which lasted three or four hours. For some days it was thought that the symptoms were due to the after-effects of the cholera toxin upon the heart. Later it was noted that the attacks came at about the same time every other day. This led to a blood examination, which revealed the presence of many benign tertian malaria parasites. Quinine treatment cured the case.

The complications and sequelæ associated with cases of malaria contracted during the war have been studied by many observers. Attention has been directed particularly to cases in which the initial symptoms were of a typhoidal type; to cases of progressive anæmia of a pernicious character with early cachexia; to the hæmorrhagic type of case; to cases of hæmoglobinuria; to cases in which the symptoms were thought to be due to adrenal insufficiency; to various types of cerebral malaria; to cases with meningitic symptoms; and to many psychical affections (malarial psychoses).

Cases illustrating a condition of ACUTE PRIMARY CACHEXIA have already been instanced. Patients suffering from this condition are emaciated and their skin and mucous membrancs are so pale as to appear almost bloodless. Weakness is extreme. The tongue is dirty, the breath foul; nausea and complete anorexia are frequently accompanied by watery or bilious diarrhœa. The liver and spleen are enlarged and tender, the urine albuminous. The subjective symptoms include giddiness, tremors, breathlessness, failure to sleep, and great depression. The arterial tension is exceedingly low and various extracardiac bruits are heard on auscultation. The count of the red blood cells is usually less than two millions per cubic millimetre and in as short a period as a fortnight or three weeks may fall below a million to as low as 500,000 or even less.

According to Paisseau and Hutinel, Armand-Delille, Lemaire, and others, MENINGEAL SYMPTOMS are sufficiently frequent in malaria for an actual malarial meningitis to be described. The complication is more frequent in children. The following is an example:—[1]

A child of 10 was admitted into hospital on the fifth day of his illness, which had come on gradually with depression, lassitude, headache, diarrhœa, and anorexia. On admission, the symptoms were prostration, intense headache, a heavily-coated tongue, gurgling in the right iliac fossa, diarrhœa, and a rapid pulse. The heart and lungs appeared normal, and the liver and spleen were not tender. There was no rash. The temperature was continuously high, with a few well-marked remissions. Five days later the child became delirious, and was stretched out rigidly "like a pointer." Stiffness of the neck, rachialgia, and Kernig's sign were marked. The child made inarticulate cries, and answered no questions. Examination of a blood-film showed numerous malignant tertian parasites. The case was fatal.

Paisseau and Hutinel state that in over 60 per cent. of cases of malaria, taken at random, a meningitic reaction in the cerebrospinal fluid can be demonstrated. The microscopic characters of the cerebrospinal fluid are generally in relation to the severity of the clinical phenomena. In an average case it is usual to find from two to four cellular elements in each field of the oil-immersion lens; but with intense meningitic symptoms, as many as twenty may be found in each field. The cells are small lymphocytes, and a few medium-sized mononuclear cells. Usually there are no polynuclear cells. The amount of albumin in the fluid is notably increased, but the pressure is generally low.

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[1] Paisseau and Hutinel in the *Paris Médical*, March 8, 1919.

It appears that in some cases the meningitic syndrome may dominate the clinical picture to such a degree as to suggest that the case is one of cerebrospinal meningitis; in other cases the signs are obscured by coma or other symptoms which are not entirely meningitic in origin.

Under energetic quinine treatment recovery from meningitic symptoms is the general rule.

PSYCHICAL AFFECTIONS occurring during the War as a sequel to malignant malaria have been studied especially by French neurologists. Porot and Gutmann, of the Neurological Institute in Algiers, have recognized a number of clinical types.[1] They maintain that the malarial psychoses are always primarily of the confusional type, which may be transformed later into various syndromes of a more advanced and protracted character. Their classification of the clinical types is under two chief headings, namely:—

(1) Acute simple confusional psychoses.
(2) Prolonged psychoses.

The first group comprises cases which are definitely and exclusively of a confusional character. The mental confusion is usually accompanied by a dullness of the intellect amounting to stupidity, and by a constant desire to sleep. The average duration of these cases is usually from one to several weeks, and the symptoms pass off in proportion as the patient recovers his general health, and becomes free from his malarial infection. If they last more than two or three months the clinical picture usually takes on the aspect of a more serious syndrome.

Under the group of prolonged psychoses Porot and Gutmann describe four chief clinical types, namely: (1) those in which the primary state of confusion becomes chronic, and sometimes passes into a condition of catatonic dementia; (2) those in which the psychical affection is associated with a continued state of bad general health resulting from an uncured malarial infection; (3) forms in which there is persistent hallucination, and the patient becomes a chronic delirious subject; (4) forms in which malaria sets in motion a latent constitutional taint of insanity.

The common psychical affection, usually termed "malarial neurasthenia," comes under the second sub-heading of this classification. Patients suffering from this condition are often persons who have been insufficiently treated during an intense primary attack, or they may be old residents in the tropics who have had many infections and reinfections, and are weakened by prolonged residence in an unhealthy country. Signs of bodily ill-health are often present, such as a chronic condition of anæmia, breathlessness, and weakness, accompanied sometimes by enlargement of the spleen and liver. Short relapses of fever may occur from time to time. The patients are weak and depressed; their intellectual capacity is dull; their mentality slow; their memory defective; their ability to concentrate on a subject lacking. The mind is confused and the character changed, melancholy and irritability being marked features. Impulsiveness and sudden fits of anger are of importance from a medico-legal point of view. The difference between these depressed states and true "delirious melancholy" is one of degree only. It is important that, however prolonged this condition may be, the prognosis under energetic quinine and tonic treatment is always favourable.

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[1] *Paris Médical*, March 30, 1918, p. 241.

It sometimes happens that a state of mental confusion, delirium or asthenia, is accompanied by neuro-muscular affections. Of these the most important is "malarial psycho-polyneuritis" (Korsakoff's syndrome), in which a state of mental confusion is associated with symptoms of peripheral neuritis especially affecting the lower limbs. In these mental cases with paralysis of the legs the symptoms usually last several weeks or months, but ultimately clear up under systematic treatment. The signs of neuritis are often obscured by the mental symptoms, especially as the effect of the neuritis is motor rather than sensory. "Bedridden, prostrate and delirious, the state of the patient's legs does not attract much attention, their weakness being attributed to general exhaustion; only systematic examination of the reflexes reveals the paralysis."

Dr. A. T. W. Forrester has analysed 116 cases of mental disease with a malarial history which occurred in the British Salonika Forces between October, 1918, and October 1919.[1] In thirty-two of the cases the mental symptoms occurred in association with an actual attack of malaria and in eighty-seven they followed repeated attacks. In both classes of case mental confusion was the most prominent symptom, and next came depression. There were eight cases of dementia præcox, six of delusional insanity and one of excitement with violence.

No reference to the psychoses of malaria would be complete without mention of certain FUNCTIONAL MENTAL STATES which are met with in patients who have suffered from malaria. Retired Anglo-Indians who have returned to England after a long residence in the tropics very commonly have the false belief that every slight indisposition from which they suffer must necessarily be a manifestation of their old malaria; and they continue in this belief to the end of their lives. To these patients—and sometimes to their medical attendants—the usual text-book statement, "once malaria, always malaria," is a sufficient and satisfying explanation.

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[1] *Lancet*, January 8, 1920, p. 16.

A more serious mental affliction (well known to experienced Army medical officers) has been met with very commonly during the recent War in the cases of soldiers who—in some instances unconsciously, in others by design—continue to nurse a complaint which entitles them to some material or fancied benefits. This affliction is less a disease than it is a mental state. It is comparable in some respects with the mental attitude often associated with railway accidents involving claims for compensation. During the war it was fostered by various circumstances of auto- and hetero-suggestion which attended the care and treatment of cases of malaria contracted in the Balkans and on other Eastern fronts. Under the title "La Paludose" the subject has been dealt with in an instructive and lucid manner by M. le Dr. Aynaud.[1]

The syndrome which has been described in England under the title "Apyrexial Rigor,"[2] is, at least in some cases, a manifestation of a mental state having origin from a similar primary cause. I have seen a patient who had a typical apyrexial rigor whenever a doctor who was not his usual medical attendant visited him; and another who responded perfectly to the suggestion made in his hearing as to the probable date and time of his next rigor. In some cases these rigors, without fever and without parasites, are apparently quite involuntary on the patient's part and beyond his control. I have in mind the case of a city barrister who has been free from fever and parasites for some months, but who still continues to suffer from what appear to be typical malarial rigors on being subjected to any unusual excitement, or even to such a customary procedure as palpation of the abdomen. It is clear that in cases of this kind (in which the continuance of the disability is a great disadvantage to the patient), the affliction is not due to the persistence of malaria parasites in the system but is evidence of the important rôle played by "suggestion" in disease. Such cases are usually in patients who have spent perhaps half their total military service in revolving through the pernicious cycle: Depot—Hospital—Special Malaria Centre—Convalescent Home—Depot—Hospital—Special Malaria Centre, &c. It is a mistake to treat a case of this type with quinine; to do so is tantamount to telling the patient that his malaria is not cured; and it serves also to give him an opportunity of demonstrating that the particular kind of malaria which he contracted in Salonika is a kind against which quinine is quite ineffective. This false belief about quinine in relation to Macedonian malaria has been a potent cause of prolonged disability.

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[1] "Paludisme et Paludose," by Dr. Aynaud. *Paris Médical*, August 8, 1918, p. 95.

[2] "Apyrexial Symptoms in Malaria," by Dr. Gordon Ward. *Proceedings of the Royal Society of Medicine*, vol. xii, (Section of Medicine), 1919, pp. 15-36.

On pp. 123-124 I gave my views as to the characters of the developed disease in the great majority of the cases of malaria invalided from Macedonia and other Eastern war areas. The above account of complications and sequelæ covers most of the findings in exceptional cases. For the rest I may note as briefly as possible the following points:—

(*a*) Although in the great majority of cases a single dose of quinine given empirically every day reduced the frequency and severity of relapses in a remarkable manner, there were certain cases in which this dose failed to prevent the recurrence of relapses. The proportion of failures was higher with a daily dose of only 5 grains than with a daily dose of 10 grains, and there were a few failures even with a daily dose of 15 grains given intravenously. The following temperature chart illustrates such a case:—

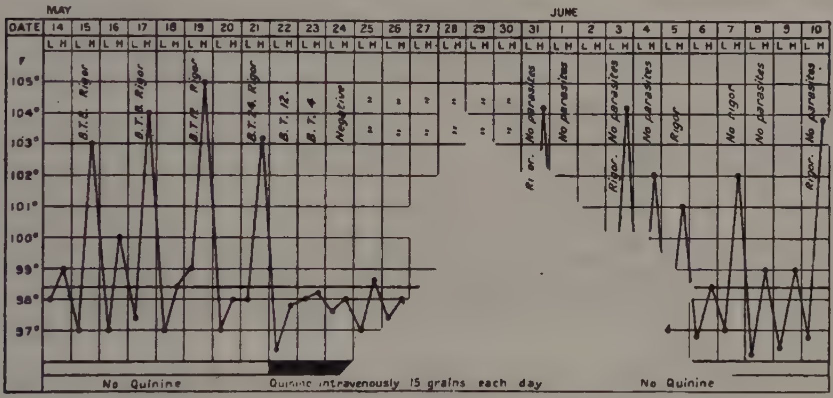

Fig. 88.

It is noteworthy in this case that the relapse began on a day on which the intravenous dose had been given and that, although no quinine was administered after the relapse began, no parasites appeared in the peripheral blood. In this and some other cases of failure to prevent relapses with a single daily dose the explanation seemed to be that the dose was not administered at the correct time for acting upon parasites in the vulnerable stage. From our knowledge of the rapidity with which quinine disappears from the blood we know that the time at which a dose is administered is all-important. In other cases of failure with a single daily dose, the explanation seemed to be that in view of the great abundance of parasites the single dose of 10 grains was not a sufficient quantity of quinine for the purpose desired. In these cases the patients suffered from slight, but true, malarial relapses with a rise of temperature to perhaps 100° F. We obtained no evidence that a race of "quinine-fast" malaria parasites was developed; and I have met with no old-standing case of malaria in which 30 grains of quinine given daily in divided doses at appropriate intervals failed to cure an ordinary uncomplicated attack within a few days.

(*b*) On the parasitological side, as well as on the clinical side, findings which appeared to be paradoxical were not infrequent. I have already mentioned cases in which there were numerous parasites without fever; cases of severe fever with few or no parasites; and cases in which the curve of fever could not be correlated with the stages of growth of the parasites which were present in the peripheral blood. Another interesting point was the great frequency of mixed infections with malignant and benign tertian parasites; indeed it almost invariably happened that patients invalided with malignant tertian parasites ultimately showed that they had been infected also with benign tertian parasites. Sometimes both kinds of parasites were present simultaneously in the peripheral blood; more commonly cases appeared for the first few months to be infections with only malignant tertian parasites, and later to be infections with only benign tertian forms, which persisted after the malignant parasites had apparently been eradicated by systematic treatment.

Another interesting finding was in connection with the character of some benign tertian parasites, especially in the stage of division or sporulation. In old-standing cases some of the full-grown benign tertian forms in red cells which were deeply stippled with Schüffner's dots were not larger than a normal blood corpuscle, and formed rosettes consisting of only ten to twelve young parasites. Moreover, the red cell in which they lay, although it was profusely spotted with Schüffner's dots, was only slightly enlarged.

As happens usually in European malaria patients under more or less regular quinine treatment, gametocytes were exceedingly numerous in many cases. In addition some forms of the benign tertian parasite have been described which bear a superficial resemblance to gametocytes, but which (it has been suggested) may possibly be an asexual quinine-resisting "latent" form responsible for relapses. J. D. Thomson and H. M. Woodcock have described and figured a form which may be of this nature, and it is possible that a similar form was seen some years ago in cases of quartan malaria in Panama.

CHAPTER VII (*continued*).

SECTION IV.

DIAGNOSIS.

A diagnosis of malaria may be arrived at :—

(1) On the result of blood examination.

(2) On the clinical symptoms and signs.

(3) On the effect of therapeutic doses of quinine.

(4) On the history of the patient's movements considered with full knowledge of the malariology of the places visited.

THE MICROSCOPIC EXAMINATION OF THE BLOOD, when carried out by a practised observer (and especially if the blood specimen has been taken before any quinine has been administered to the patient), is the surest and best method of arriving at an accurate diagnosis. In every case of fever suspicious of malaria (even if the probability of its being malaria is remote) a blood film should be taken and examined at the first opportunity. Until the blood film has been taken quinine should not be administered.

In the paragraphs on deaths from malaria (p. 149), I gave particulars of two cases in which it is probable that a fatal issue might have been prevented if blood specimens had been taken and examined at an early stage. These cases, as well as the remarks on pernicious symptoms (p. 153), should serve to justify the contention that in all doubtful cases of fever the medical practitioner's first diagnostic rule should be to take a blood film.[1]

The method of taking, staining, and examining blood films has already been described (Chapter III, p. 20, and Chapter VI, p. 97), but it will be useful to supplement that description with the following details :—

(*a*) Working with a well-stained thin film the examination of 100 fields occupies on an average ten minutes when the film contains parasites, and from five to seven minutes when no parasites are present. At least 200 fields should be examined before recording a result as "negative."

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[1] In England the Ministry of Health have made arrangements by which such blood specimens will be examined and reported on free of charge. The specimens should be addressed to the Ministry of Health, Whitehall, London, S.W.1, accompanied by the patient's name, and the name and address of the sender.

(*b*) The following figures taken from the records of routine examinations show that parasites are somewhat more numerous along the edges than along the centre of a thin film :—

Number of fields examined	Area of film examined	Number of parasites found	Time occupied
100	Along the upper edge of film	83	11 minutes
100	Midway between upper edge and centre ..	71	12 ,,
100	Along centre of film	67	8 ,,
100	Midway between centre and lower edge ..	70	8 ,,
100	Along lower edge of film	99	12 ,,
Total .. 500		390	51 minutes

(*c*) Working with Leishman's stain made up from the crystals supplied by Messrs. Baird and Tatlock, we find that it is best (in order to bring out Schüffner's dots, etc.) to leave the undiluted stain on the film for one minute, then to dilute with an excess of distilled water, and to allow this mixture to remain on the film for twenty minutes.

(*d*) When the routine is to examine only one thin film from each case, it is known to workers in the tropics that, taking one case with another, it is not usual to find malaria parasites in more than about 40 per cent. of true malaria cases. Most of the negative results are due to the circumstance that quinine has been given before the film was taken, or to the film having been taken during an apyretic interval, but, even in quite untreated patients suffering from fever, parasites may be too rare to be found at a single examination. This often happens during the first two or three days of a comparatively mild primary infection, and we have to admit that at this highly important period of such cases a single blood examination sometimes fails to help us in diagnosing the case. An example of this has been recorded on p. 115, and another on p. 152. The search may also fail during short relapses in persons who have acquired a relative immunity, even when such persons have enlarged spleens and other physical signs of malaria.

The failure is due to the fact that the amount of blood which we can examine in a reasonable time is exceedingly small. Various plans have been suggested for increasing the amount of blood which can be examined in a given time. The simplest, and in our experience the most satisfactory, is to cover the whole of the blood film with a thin layer of cedar-wood oil, and (without applying a cover-glass) to examine it with a ⅙-inch objective and No. 6 eyepiece. Provided that the film is clean and well-stained, even small rings can be readily detected under this magnification, and, because the film is already covered with oil, the nature of any doubtful object can be quickly ascertained by turning on the oil-immersion lens.

Another plan is called *the thick-drop method.* It may be carried out in a simple way as follows:—

(1) Sterilize the patient's finger, or lobe of the ear, and draw blood with a "pricker."

(2) Pick up a perfectly clean dry slide and take upon it four small drops of blood so that they will be at the corners of a small square (½ in. by ½ in.) as shown in fig. 89.

(3) With a glass rod join the four drops together so that the blood lies in an even layer as in fig. 89. Do not "puddle" the blood unnecessarily.

Fig. 89.

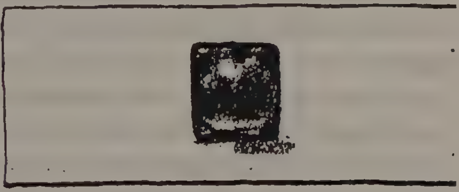

Fig. 90.

(4) Lay the slide *flat* on the level floor of a dust-free box or drawer, and leave it until quite dry. This occupies about an hour.

(5) Dehæmoglobinize the blood by placing the slide upright in a glass of tap water. Dehæmoglobinization is usually complete in about ten minutes. When the slide is removed the square of blood should appear white.

(6) Without waiting for the blood to dry, and without fixing, stain in the ordinary way with Leishman's stain, or with Giemsa's stain, or by placing the slide in a glass staining jar containing the hæmatin stain described on p. 31. The procedure of dehæmoglobinizing, staining and washing, should be carried out gently so as not to wash off the unfixed layer of blood.

(7) Allow the specimen to dry in the air (do not blot it) and examine with the oil-immersion lens in the ordinary way.

Some workers dehæmoglobinize with acid alcohol and stain with methylene blue and eosin; others dehæmoglobinize with dilute alcohol (30 per cent.) followed by fixation with absolute alcohol. Whatever procedure is employed, the thick-drop method as a whole is crude, and provides opportunities for many diagnostic errors. It should be employed only to supplement the ordinary thin film method, never as a substitute for that method. When a large number of cases have to be examined the following is a good plan:—

(*a*) Make two thin films and one thick-drop preparation from each case.

(*b*) After careful labelling, or otherwise marking for identification, hand over the thick-drop preparation and one of the thin films of each case to an assistant.

(*c*) Stain and examine the other thin film of each case. If parasites are found in this film the thick-drop preparation and the second thin film may now be discarded. If parasites are not found the assistant should be instructed to dehæmoglobinize and stain the thick-drop preparation and to stain the second film. Usually these specimens are ready for examination on the afternoon of the day they were taken. Examine the thick-drop preparation first. If it is negative do not examine the second thin film. If the thick-drop seems to contain one or more parasites search the two thin films until a parasite is found.

I have already mentioned (p. 98) that the thick-drop method is not applicable to field work in the open. Even for diagnostic work in properly equipped hospitals and laboratories I hesitate to recommend its use except when controlled by the plan described above.

Evidence of malaria when parasites cannot be found. The following notes are supplementary to the remarks made on p. 28 :—

(*a*) The discovery of true malaria pigment in a white cell in the peripheral blood is as good evidence of present or recent malaria as if an actual parasite had been found. Indeed it usually happens that when grains, rods or blocks of pigment have been found in a white blood cell, further search of the film results in the discovery of a parasite.

(*b*) In recent years both the total count of the leucocytes and the "differential leucocyte count" have lost some of the importance which was formerly attached to them for purposes of diagnosis. To be of much value both the total count and the differential count must be carried out; and if possible they must be repeated on two or more succeeding days and correlated with the temperature and other clinical signs. The usual leucocytic changes have been described on pp. 135 and 136. Leucopenia is in favour of a diagnosis of malaria, but an increase in the total number of leucocytes has been a common finding at single examinations of patients who are still suffering from the after effects of malaria contracted during the War, the increase being almost entirely in lymphocytes.

When making differential leucocyte counts it is important to remember that the polymorphonuclear cells have a greater tendency to be dragged to the edges and end-tags of the film than the lymphocytes. For this reason the result of a count which is confined to the straight edges of a film may be different from the result of a count made in the middle areas of the film. The best way to minimize errors of this kind is to take only a very minute drop of blood and to examine every part of the film made from it.[1] By doing so we make sure of obtaining the correct proportions of the various leucocytes present in that particular drop of blood. A second small drop should be examined if sufficient leucocytes (at least 300) are not present in the first.

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[1] An ordinary thin film contains several thousand leucocytes. A drop less than the size of a small pinhead should be taken.

(*c*) The presence of macrophagocytic cells in the peripheral blood is a better diagnostic sign of malaria than is a change in the relative proportions of the leucocytes. The character of the usual types of these cells has been mentioned on p. 136, and a few are shown in fig. 91. Possibly they are derived from the vascular endothelium.

(*d*) Neither the finding of unequivocal macrophagocytic cells, nor the results of a total and differential count of the leucocytes, can be regarded as a sure sign that the patient is suffering from malaria, but the results of observations on these subjects by an experienced worker are a considerable aid in difficult cases when taken in conjunction with the history and the clinical signs and symptoms. The finding of parasites, or true malarial pigment, are the only sure microscopical signs that a patient is suffering from malaria.

Among the CLINICAL SIGNS the important diagnostic character is periodicity of a tertian or quartan type. If the fever, OR ANY OTHER SYMPTOM, recurs at stated intervals of approximately 48 or 72 hours, the disease is almost certain to be malaria.

If the periodicity is quotidian the matter is quite uncertain. Suppuration in any part of the body, tuberculosis, and many other diseases or conditions may produce daily rises of fever, accompanied by rigor and sweating. It is many years since Professor Thayer wrote that "the one process above all others which is confounded with malarial intermittent fever is pulmonary tuberculosis," and Sir Patrick Manson has said much the same as regards liver abscess: "At one time or another, most liver abscess cases are drenched with quinine, on the supposition that the associated fever is malarial." Nevertheless, there is one type even of quotidian periodicity from which a moderately certain diagnosis of malaria may be made, namely, the type in which the daily febrile paroxysm comes on before midday. If a patient has an attack of fever beginning at about the same time each day, between 2 a.m. and 11 a.m., he is very likely to be suffering from malaria.

THE EFFECT OF THERAPEUTIC DOSES OF QUININE as a test of malaria is useful as a last resort when other methods of diagnosis have failed, but it should not be used as a routine method of endeavouring to arrive at a diagnosis. *A case of fever that resists doses of ten grains of quinine given in solution three times on two successive days is most probably not an ordinary case of malarial fever.* This is the only deduction that can justifiably be made from the test. One must not conclude that a patient whose temperature has declined after receiving this treatment is necessarily suffering from malaria, because his disease might have been one in which the temperature would have fallen whether he had received the quinine or not. Therefore the test is useful only as a method of excluding malaria; and it should be used with caution, because large doses of quinine are harmful to patients suffering from such diseases as typhoid fever, tuberculosis, &c.

In malarious countries it is a common observation that diseases are diagnosed

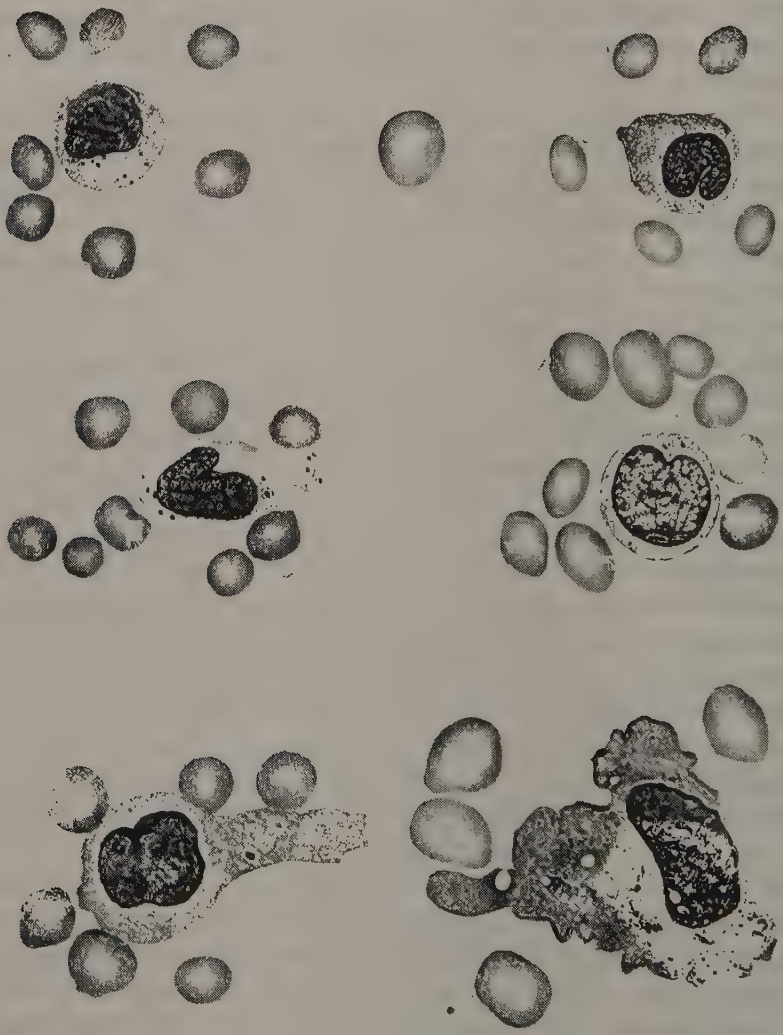

FIG. 91.

as malaria when they are not due to that cause. In those countries most patients who complain of "fever" express the opinion that the fever from which they are suffering is "malarial," and unfortunately many tropical practitioners all too frequently acquiesce in this opinion without taking pains to ascertain its correctness. In such instances the medical man, having allowed the patient to make the diagnosis, usually proceeds to treat him more or less vigorously with quinine. If, under this treatment, the fever disappears in a few days, the medical man regards the diagnosis as having been confirmed: he has applied what is called the "therapeutic test." But if the fever does not decline within a few days, the results of having adopted a wrong method of diagnosis become apparent, and often several weeks elapse before a correct diagnosis is reached.

In non-malarial countries, on the contrary, recent experience is to the effect that cases of malaria are frequently diagnosed under the heading of some other (often obscure) disease. The following is a list in alphabetical order of some provisional diagnoses made in England and other non-malarious countries in regard to cases subsequently proved to be malarial:—

Anæmia and debility.
Aphasia.
Appendicitis.
Cerebrospinal fever.
Coma.
Convulsions.
Disordered action of the heart.
Dysentery.
Dyspepsia.
Epilepsy.
Hæmorrhagic pancreatitis.
Influenza.
Jaundice.
Neuralgia and neurasthenia.
Plague.
Pyrexia of uncertain origin.
Rheumatic fever.
Sandfly fever.
Simple continued fever.
Trench fever.
Typhoid or paratyphoid fever.
Valvular disease of the heart ("septic endocarditis").
Worms.
Yellow fever.

On the other hand, of course, it must not be forgotten that in England, as in the tropics, it has happened that in known malarial subjects all the symptoms in a serious illness have been thought to be due to malarial infection, when more thorough examination would have revealed the presence of another illness to which in part, or in whole, the serious symptoms were due.

Malaria is one of the diseases in which a careful inquiry into the HISTORY of the patient's previous movements is often of great assistance in diagnosis. See for example the cases recorded on pp. 110 and 112.

Remarks on Cases which may be difficult to diagnose.

Especially in the tropics, many cases of "fever" occur in which the diagnosis of the cause of the fever is difficult. Let us suppose, for example, that a patient is examined on the second day of his illness, that the temperature is 102° F., that his spleen is not at all, or only very slightly, enlarged, and that a thorough examination of the respiratory, alimentary, circulatory, genito-urinary, nervous and glandular systems has failed to reveal the presence of any local affection which would account for the fever. In such a case the correct course to pursue might be stated as follows: (1) admit the patient to hospital; (2) allow him only milk diet; (3) give instructions for his temperature to be taken at least every four hours, preferably every two hours; (4) withdraw 5 c.c. of blood under strictly aseptic precautions from a vein and transfer 3 c.c. to a bottle of blood culture medium for dispatch to the laboratory; (5) take also a capsule of blood for serum reaction tests and make two thin films and one thick drop preparation to be examined for malaria parasites; (6) if thought desirable, a diaphoretic mixture and a mild purgative may be prescribed, but quinine should not be given.[1]

The blood specimens should now be dealt with, no time being lost in examining the blood films for malaria and other blood parasites. If it happens that we find the parasites of malaria, or of relapsing fever, or of filarial fever, in the blood, the task of diagnosis is ended and appropriate treatment can be begun at once. If microscopic examination gives a negative result we must await the results of the procedure for blood culture and serum reactions. In cases of typhoid fever, diagnosis by blood culture can be made on the first or second day of the disease; it may be said also that in cases simulating typhoid fever, but in which the results of culture with a blood specimen taken during the first three days of the fever are negative, typhoid fever may be excluded. During this period, and subsequently until a sure diagnosis can be made, the course of procedure is one of watchful expectancy for some positive symptoms and signs which will afford a clue to the correct diagnosis. An examination of the blood for malaria parasites should be made at least once each day, and the rule not to give quinine until the diagnosis is established should be adhered to. When this plan is pursued it will be found that, if the result of blood culture is negative, one or other of the following events happen: (1) Within at longest seventy-two hours the temperature chart and the patient's symptoms show definitely the character of intermittency, perhaps also that of periodicity; (2) neither the temperature nor the symptoms show features of diagnostic significance, but malaria parasites are found in the blood. In either of these events quinine treatment should be begun at once. (3) The temperature is irregular, but shows a tendency to fall from the first or second day. Within four or five days it has fallen to normal and the patient has recovered. No malaria or other parasites are found in the blood and blood culture and serum tests are negative. In this event the diagnosis of the true cause of the fever remains unknown and we must return the case under the heading "pyrexia of uncertain origin." (Perhaps we may call it "heat stroke" or "three-day fever" or "seven-day fever" or "sandfly fever" or "influenza," or any other name which seems appropriately to fit such symptoms as may be present.) (4) Repeated blood examinations for malaria are negative, but the temperature chart shows a more or less high temperature day after day with or without remissions. In cases of this nature we can definitely exclude malaria after four or five days at the latest, because we know both that a malarial patient who had received no quinine could not continue to have high fever for more than two days without our being able to find parasites in his blood, and that the temperature chart of a case of malaria (when no quinine has been given and when the temperature has been taken sufficiently often) always shows within a few days the intermittency (and usually the periodicity) characteristic of the disease.

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[1] The teaching that, having obtained specimens of blood, we should begin at once to treat the patient with quinine "on the chance" that he may be suffering from malaria is justifiable in exceptional circumstances only. In the vast majority of cases of fever the advantages to the patient of waiting until malaria can be definitely diagnosed, or definitely excluded, far outweigh any which can be brought forward in favour of giving quinine at an earlier stage.

When a week has elapsed without a definite diagnosis being indicated, blood culture is no longer useful, but the serum reaction tests for typhoid and paratyphoid fevers and for Malta fever should be tried again. If their results provide no clue and the temperature is still continuous or remittent, or perhaps even intermittent with a quotidian periodicity, we should consider again the possibility of tuberculosis or liver abscess, or some other septic condition, going carefully over each anatomical system (not failing to examine the ear, the throat and the nose) and employing such bacteriological methods as are available for the examination of sputum and swabs. We should make a thorough examination of the urine, search the fæces for amœbæ and the eggs of intestinal worms, and consider the possibility of syphilis and whether it is advisable to examine the cerebrospinal fluid. Perhaps at this stage a total count of the leucocytes, together with a differential count, may provide an important clue to some inflammatory condition.

Finally we may be compelled to think of the imperfectly known continued fevers and of kala-azar. If the case is one of kala-azar we shall note rapid progressive enlargement of the spleen until it attains a size never reached in cases of typhoid or Malta fever. This brings us to the consideration of the class of diseases in which enlargement of the spleen may be very great. It often happens in the tropics that patients present themselves at a hospital for the first time with a spleen so large that it extends to or beyond the level of the umbilicus. In such cases the diagnosis, when chronic Bright's disease, cirrhosis of the liver, and syphilis, have been excluded, usually rests between splenic leukæmia, chronic malaria, and kala-azar. The patients may or may not have fever at the time of admission to hospital. In such cases the first thing to do is to make a complete examination of the peripheral blood as regards both total and differential counts of white cells, and total count, estimation of hæmoglobin, search for parasites, etc., of red cells. The exact condition of the anæmia will thus be ascertained, and on the results of repeated examinations for this object we can at least make a provisional diagnosis which will give an indication for appropriate symptomatic treatment. The differential diagnosis between chronic malaria and kala-azar is not always easy at a single examination, and we may have to admit the patient into hospital and observe him for some time. The chief clinical differences between the two diseases may be stated as follows:—

Chronic Malaria.	*Kala-azar.*
There are definite pyrexial and apyrexial periods: the pyrexial periods are of short duration and if a careful record of the temperature is taken every four hours the chart presents definitely (in the absence of quinine treatment) the characters of a malarial chart. Quinine stops the fever.	Fever is present for long periods; it is sometimes intermittent but shows great irregularity. Quinine does not stop the fever.
Progressive emaciation is rare, and between the pyrexial attacks the patient is able to do his work. The spleen is greatly enlarged; the liver only slightly or not at all.	Great weakness and progressive emaciation are always present. Both the spleen and liver are greatly enlarged.

The examination of the peripheral blood for parasites only sometimes yields results which aid the differential diagnosis between these two diseases. In chronic malarial patients who have suffered from repeated infections and reinfections for perhaps ten or twelve years, malarial parasites are often very scanty and appear in the peripheral blood for only a short time during the pyrexial attacks. They can be found more frequently (though by no means invariably) by withdrawing a little blood from the spleen. This procedure is not justifiable as a routine method of diagnosis, but in a few cases it may be necessary to resort to it. It provides at once a positive diagnosis in cases of kala-azar by revealing the presence in the splenic endothelial cells of numerous Leishman-Donovan parasites which are the cause of the disease.

The diagnosis of pernicious attacks of malaria is sufficiently dealt with in the descriptions which have already been given on pp. 152 to 166. In such cases it is seldom possible to save the patient's life unless we are able to make an immediate examination of the blood, because until this is done the diagnosis is often obscure and the treatment quite incorrect.

Diagnosis between True and False Malaria.

On p. 167, I mentioned the mental state which has been described under the title "La Paludose." The diagnosis between this affliction and true malaria is not always easy. In connection with it a particular diagnostic problem which has become of importance since the war may be stated as follows: When a person who has been resident in a non-malarious country for several years states that he still suffers from malarial attacks, what steps should be taken to make a correct diagnosis of his illness?

From the point of view of treatment the matter is important, because it does more harm than good to treat a patient whose symptoms are the result of a false belief, as if they were due to the persistence of malaria parasites in his system.

In considering the diagnosis of this class of case it must be remembered first that there are quite a number of authentic cases in which true malarial relapses with parasites (*P. vivax*) in the peripheral blood occur two years after an infected person has left a malarious country; and that there are a few cases in which true relapses occur three years after. Beyond this period the occurrence of a true relapse is a rare event which always merits careful study. A patient whom I have seen was repeatedly infected in Palestine in 1916, and arrived in England in February, 1917. He had a true relapse with parasites in January, 1920. He admits that he has always tried to avoid taking quinine, which he believes may cause permanent deafness and loss of sight.

If, at a single examination, there has been failure to find malaria parasites or true malarial pigment in the blood of a patient who, after more than two years' residence in a non-malarial place, states that he still suffers from malarial relapses, the best step to take is to arrange for daily observation until a diagnosis can be made. Quinine should not be given during this period of observation. For purposes of diagnosis no reliance should be placed upon the statement of symptoms made by the patient, nor upon any method of examination in which the patient has to collaborate by answering questions or making signs indicative of pain or tenderness. The temperature should be taken at the usual intervals, but as a general rule it is best to rely almost entirely on careful physical examination and on microscopic work frequently repeated.

We must keep constantly in mind that the patient may possibly be suffering from some other condition than malaria, such as tuberculosis or syphilis, or perhaps that he may be in the early stage of liver abscess. If repeated examinations of the fæces, urine and sputum are negative and there is no evidence of enlargement of the liver, we are justified (at a period not less than two years after arrival in a non-malarious country) in suspecting that a patient who states that he is frequently incapacitated from work by malarial attacks may be suffering from a functional mental condition. In these circumstances a complete blood examination, repeated at the same hour every two or three days during a period of ten days or a fortnight, is sometimes of great value. The following is an example of the use of this method in a patient who had been two years in England. When first seen he stated that he had had a rigor a few days previously, but we detected no physical sign which was confirmatory of his statement. He agreed to attend at 10 a.m. daily for blood examination. The following is a sufficient statement of the results. No quinine was given during this period.

In this case the results did not enable us to state that the patient was suffering from malaria, but they showed clearly that the condition of his blood was by no means normal. For our immediate purpose this was sufficient; it proved that the patient had a definite disease.

	1.11.19	2.11.19	4.11.19	6.11.19	8.11.19	11.11.19	15.11.19	17.11.19
Parasites	0	0	0	0	0	0	0	0
Hæmoglobin ..	70 %	—	74 °/o	—	72 °/o	—	76 °/o	—
Total red cells ..	5,150,000	—	5,500,000	—	5,250,000	—	—	—
Total leucocytes ..	9,500	15,400*	8,437	12,000	14,375*	9,000	8,500	10,625
Differential count—								
Polynuclears ..	50 %	51 %	46 %	53 °/o	53 °/o	50 %	50 °/o	52 %
Mononuclears ..	49 %	47 %	53 %	46 °/o	47 °/o	49 °/o	50 °/o	48 %
Eosinophils ..	1 %	2 %	1 %	1 °/o	—	1 °/o	—	—

* Repeated with practically tbe same result.

In some other cases of the same and longer duration, repeated blood examinations carried out as in the above case yielded on each occasion a result indicating, that, so far as could be ascertained, the blood was quite normal. One of the patients whom I have already mentioned as being the subject of "apyrexial rigors," was also an example in which the rigors were not followed by any detectable change in the hæmoglobin index of the blood or in the total and differential count of the leucocytes. He was a well educated man of an emotional temperament, who had spent by far the greater part of his war service in hospital. He held firmly the conviction that his was a particularly "interesting case," from which something unusual was to be expected. In this expectation he seldom failed to disappoint himself or his medical attendants. After providing an example of many of the paradoxical findings which have been recorded in the literature of malaria during the war, he began to complain of suffering frequently from diarrhœa. The last available news concerning him stated that he was in one of the special hospitals which had been established for dealing with "amœbic carriers."

Some consider that in a few cases of suspected malaria it may be justifiable for diagnostic purposes to endeavour to bring on a relapse—or at least to employ a procedure which will result in the appearance of parasites in the peripheral circulation in which they can be detected by microscopic examination. The subcutaneous or intramuscular injection of normal serum, milk, strychnine, iron, iodides, salvarsan, ergotine and adrenaline, as well as various plans for inducing a "chill" (cold douches to the abdomen, &c.) are among the so-called "provocative methods" which have been employed with that object. The injection of adrenaline (1 milligram subcutaneously) is said to give the highest percentage of positive results. I have no personal experience of these procedures, and, except for purposes of experimental research, the circumstances in which it is desirable to utilise them must be quite exceptional.

CHAPTER VIII.

TREATMENT.[1]

QUININE is an effective remedy for an attack of malarial fever. Its administration should be begun immediately the diagnosis is assured, irrespective of the stage of the attack or the height of the fever. But, unfortunately, the cure of the attack is seldom or never accompanied by complete eradication of the parasites, and we have to admit that up to the present time, quinine treatment, in whatever manner it has been carried out, has not fulfilled the hope that it would prove to be a *therapia magna sterilisans.* Doubtless the success of the drug in curing attacks depends on a number of factors: and perhaps its frequent failure to prevent recurrences is due less to the inefficiency of the drug than to our ignorance of the correct way in which to use it. We know little or nothing about these subjects. There is as yet no sure answer to the question whether quinine, when given in therapeutic doses, acts directly on the parasites by poisoning them, or whether it brings about their destruction in an indirect way. If it acts simply by a direct killing-effect on the parasites, it is strange that a dose of quinine does not have the same effect on trypanosomes and other blood parasites which, in experiments made *in vitro*, can be killed by quinine as easily as the malarial parasites. We believe that the time of administration of quinine is all-important, because we can observe that the drug is immediately effective against only one stage of growth of the parasites, namely the stage which follows sporulation; it is less effective against the older stages of growth and it is entirely inoperative against the sexual forms. Even in directing the attack upon the most vulnerable stage of the parasite, we have still much to learn. We must know first as regards the parasites: (1) In what parts of the organism does sporulation occur, and does it occur in any positions which cannot easily be reached by quinine? (2) How long before the beginning of fever does sporulation commence? (3) How long does it last?—and second as regards quinine: (1) Do we require the drug to be present in the peripheral blood, or in the internal organs, or in both? (2) How soon after administration by different methods will the drug be present in the parts of the system where it is required? (3) When will its actions in these situations be greatest? (4) How long will it remain there? (5) In regard to these points what are the differences according as we administer the drug in large or small doses, and according as we administer the amount in a single dose or in divided doses, and according as we administer it by different routes? (6) What is the smallest dose that will be sufficient to kill all the young parasites of a given generation? (7) The same number of sporozoites being injected by a mosquito into a child as into an adult, what relative doses must we employ for children and adults respectively? (8) What is the relative value of different salts of the alkaloid, and of different ways of dispensing it?

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[1] *Note.*—For brevity, symptomatic and accessory treatment are not described.

The answer to most of these questions lies in a more complete knowledge than is yet available of the physiological chemistry relating to the absorption, metabolism and elimination of quinine by the human body. The subject is complex and difficult: and the results of experimental observations by different workers do not agree. Nevertheless, everyone who tries to cure or prevent malaria by the use of quinine should know the following tentative conclusions. They help to explain some of the successes and some of the failures in various schemes of quinine treatment and prevention. (1) Quinine when administered by the mouth is absorbed chiefly in the stomach and small intestines. Absorption is rapid and complete, and observers generally are agreed that preparations of the drug which are insoluble in water are absorbed as completely, if not as rapidly, as the most soluble salts. (2) By far the greatest proportion of the quinine administered is absorbed during the first six hours after administration; the process is somewhat less rapid when the drug is given on a full stomach. (3) From the alimentary canal the drug passes into the blood, but the length of its stay in that fluid is very short, a large proportion being quickly deposited in various organs (chiefly the liver, gall bladder, kidneys, suprarenal bodies, brain and spleen), in which, but chiefly in the liver, the quinine molecule is split up and the drug destroyed. (4) The quinine which escapes destruction in the liver and other organs passes through the circulatory system and is eliminated in an unchanged condition in the urine, where it can be detected as early as twenty to thirty minutes after a dose has been taken. The elimination is greatest during the first six hours. (5) It is not known whether the quinine which is stored up and metabolized in the organs takes part in the destruction of parasites or not; most observers consider that it does not, and that the only useful portion of a dose of the drug is the portion which escapes destruction in the organs and passes through the circulatory system.[1]

The results in regard to the quick absorption of quinine and its quick disappearance from the blood indicate the paramount importance of ascertaining, for each case of malaria, the particular time at which the drug should be administered in order that it may act effectively on the vulnerable stage of the parasite. Probably in any scheme of quinine administration this is the most important point to consider.

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[1] It has been proved that "quitenine," which is one of the products of the destruction of quinine by the liver, has no therapeutic action against malaria parasites.

For the practical purposes of clinical work it is a good rule to treat patients as if it were true that: (1) Sporulation begins about two hours before the patient shows definite symptoms of rigor and fever; (2) the effect of a dose of quinine by the mouth begins in less than half an hour after administration and lasts not more than six hours. The well recognized efficacy of the old plan of giving a large dose of quinine three or four hours before an expected attack lends support to this practical rule. When more than one group of parasites is present in the blood, or when (as in malignant tertian infections) sporulation occurs at irregular intervals, the repetition of doses at short intervals is the only plan by which we can ensure that the drug will be in the blood whenever forms resulting from sporulation appear, and will continue to be present throughout the whole period during which sporulation lasts. This plan, in which a dose of three or four grains of quinine is given every two hours throughout a period of twenty-four hours, is sometimes called "the fractional method of Nocht."

If it is correct that a dose of quinine taken orally is effective for only about six hours, it is clear that a single daily dose, however large, given say at 10 a.m., will not cure a patient whose attacks always begin say at 10 p.m., or later; also that a so-called "prophylactic dose" at breakfast-time can have no effect upon the sporozoites which a mosquito may inject during the coming evening.

We know less about the fate of quinine in the human body when it is given intravenously, or intramuscularly, or subcutaneously, than we do about its fate when given orally. Clinical observations indicate that a dose of quinine given intravenously *at the correct time*, is the quickest and surest way of curing an attack and of causing the parasites to disappear from the peripheral blood. From this, one assumes that the useful portion of a dose of quinine is the portion which passes through the circulatory system, and that the object to aim at in quinine treatment is to attain as quickly as possible a high concentration of the drug in the blood. But it is known that when quinine is given intravenously, its action is more fleeting than when given by other routes.[1] For this reason unless the administration of an intravenous dose can be timed correctly in relation to the parasites, it is always wise to supplement it as soon as possible by doses given orally.

Lastly, it may be noted that quinine appears to have little effect upon parasites contained in red corpuscles which are lying more or less stagnant in the small capillaries of the deeper structure of internal organs and tissues; it is chiefly effective against parasites which are being carried freely through the circulation, especially of the peripheral parts of the body.[2]

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[1] See an article by the author in the *Journ. Roy. Army Med. Corps*, September, 1917, p. 317.

[2] The *Annals of Tropical Medicine and Parasitology*, vol. xiii, No. 2, July, 1919, contains evidence bearing on the possibility that in the blood-vascular system there are regions which are kept almost free from quinine throughout a period of quinine treatment.

We may now state certain general rules for routine quinine treatment which receive support from the above considerations, but are based chiefly on the results of well-tried clinical experience:—

(1) The administration of quinine should be begun immediately the diagnosis of malaria is assured, irrespective of the stage of the attack or the height of the fever.

(2) The drug should be given by the mouth whenever it can be administered and absorbed by that route.

(3) It will not act efficiently (*a*) if the liver is sluggish or congested; (*b*) if the alimentary canal is coated with mucus, or is otherwise in a disordered state; (*c*) if given in the form of coated tablets or pills which usually pass through the alimentary canal unchanged; (*d*) if the patient tries to carry on his daily occupation while undergoing treatment for an attack.

(4) To obviate these difficulties: (*a*) a smart purge should be given on the day on which the quinine treatment is begun; probably a dose of 2 or 3 grains of calomel, followed in a few hours by a sufficient dose of salts, is best; (*b*) the quinine should be administered *in solution*, and in a prescription which will make the taste less disagreeable, and will aid absorption and the normal working of the digestive functions; (*c*) the doses of quinine should be dispensed in a large amount of fluid rather than in concentrated form; if the administration of the drug in concentrated form, or in powder, tablet, or pill, is unavoidable, the dose should be followed at once by a wine-glass of water, acidified with a few drops of hydrochloric acid. Unless a tablet or pill can be easily crumbled between the fingers, or easily divided with a knife, it is usually ineffective; (*d*) the patient should remain in bed until the treatment of the attack is completed.

(5) The treatment of a case includes:—

(*a*) Treatment of the attack.

(*b*) "After-treatment."

The latter is as important as the former, and every medical man who has had charge of a malarial patient in England should endeavour to keep in touch with him for at least two years after the primary attack. When the disease has been overcome, apparently for good, it may occasionally show itself in one or other of a variety of unexpected ways, which may seem to be quite unconnected with the original infection.

(6) For the treatment of the attack, in addition to following Rules 1 to 4, the most important matter is that, however mild the attack may be, the patient should go to bed and remain there for at least three days, and, preferably, for five days, whilst he is going through the course of quinine treatment prescribed. A routine plan which has proved satisfactory for the treatment of most attacks in adults is to give three times daily on five consecutive days 10 grains of the sulphate or

hydrochloride of quinine dissolved (with dilute acid) in at least 2 ounces of water. A better plan (which takes into consideration the opinion that the action of a dose of quinine lasts only six hours) is to divide the 30 grains of quinine, which must be given during each twenty-four hours, into four doses instead of three, and to give these doses at the following times: 12 midnight, 6 a.m., 12 noon, and 6 p.m. By following this plan we are more likely to ensure that there will be a sufficient concentration of quinine in the blood at the time when the youngest forms of the parasite are present. In the majority of cases of malaria it happens that the febrile paroxysm (which follows sporulation of the parasites) begins between 2 a.m. and 12 noon; and it is for this reason that the doses at 12 midnight and at 6 a.m. are so important. As a general rule, however, it will be found that either of the plans just mentioned causes the parasites to disappear from the peripheral blood, and the fever to cease within twenty-four to seventy-two hours, but the treatment should be continued without fail for five days. This completes the cure of the attack.

(7) Occasionally in malarial attacks vomiting is so persistent that it is useless to give quinine by the mouth, nor can it be so administered in some pernicious attacks, when no time must be lost. In such cases the best method of treatment is to administer the quinine *intravenously*. This operation is not difficult, but it requires good technique, great care, and strict aseptic precautions.

Method of Administering Quinine Intravenously.—The following articles are required for the administration: (1) An all-glass syringe of 5 c.c. capacity, and with a new needle, which must be very sharp; (2) tablets of a salt of quinine soluble in water, preferably quinine bihydrochloride; (3) a spirit lamp, tripod stand and porcelain dish; (4) test-tubes, filter papers, alcohol and lint, and a pair of forceps; (5) normal saline solution made up with pure distilled water; (6) a measure glass marked in cubic centimetres. All the articles with which the injection is made should be thoroughly sterilized before use, and the patient's arm rendered aseptic.

The following are the details of the operation: (1) In a sterilized measure glass dissolve 15 grains of quinine bi-hydrochloride in 5 c.c. of normal saline solution; (2) filter it into a sterile test-tube and boil it; (3) if quite clear, pour into the sterile porcelain dish and draw it up into the syringe, which it should completely fill; (4) the patient should be lying in bed. By applying a bandage, make the median basilic vein as prominent as possible. Do not attempt the operation unless the vein is standing out prominently; (5) see that the needle of the syringe is firmly attached, and that it is completely filled with the quinine solution; (6) let a drop of the solution fall on the skin over the vein at the spot selected, and through it pierce the skin and the anterior wall of the vein; (7) turn the needle point towards the patient's shoulder and push it onwards until at least half the needle is lying freely in the lumen of the vein; (8) remove the bandage and let the arm be relaxed so that the blood in the veins can flow freely; (9) make certain that the needle is in the lumen of the vein by withdrawing a few drops of blood into the syringe; (10) if this is the case, without moving the point of the needle, inject very slowly 1 c.c. of the solution and wait a few moments. If the needle is correctly in the vein, there will be no swelling at the site of injection, and the patient will feel no pain there; (11) inject slowly another cubic centimetre and wait again, and proceed in this manner until all the solution is injected.

The two most important points are that the needle should be in the lumen of the vein and that the injection should be made very slowly. If the needle misses the vein, or slips out of it, stop the injection at once, and, before withdrawing the needle, suck back into the syringe all the solution that may have escaped into the subcutaneous tissue round the vein. Then with another syringe and fresh solution make the injection into another vein.

One dose of 15 grains given intravenously is usually sufficient to stop the fever and to cause the disappearance of most of the parasites within eighteen hours. Vomiting and other acute symptoms usually subside within a few hours, so that quinine can then be given by the mouth in the manner described above. If vomiting still persists, a second injection should be given six hours after the first.

When quinine cannot be given by the mouth, and if one is not prepared to give it intravenously, the next best thing to do is to administer it intramuscularly. The arrangements are the same as for intravenous injection, but it is advisable to dissolve the 15 grains in 10 c.c. (or even in 15 or 20 c.c.) instead of in only 5 c.c. of saline and to inject half into the gluteal muscle and half into the deltoid. The site of injection must be carefully selected as far as possible away from the main branches of nerves. The needle should be thrust deeply into the muscle at right angles to the skin. After the solution has been injected, and the little wound closed with collodion, the part should be gently manipulated and massaged. This, as well as the high dilution of the drug, aids rapid absorption and prevents precipitation at the site of injection.

Quinine may also be given subcutaneously, but, at any rate in India, it has long been the experience of most medical officers that injections given intramuscularly are preferable.

The objection to both the intramuscular and subcutaneous methods of administration is that they are sometimes followed by local necrosis and abscess, or by injury to nerves. During the war many quite serious troubles of this nature occurred, especially after injections which were described as having been given subcutaneously. When this is the selected route great care should be taken to see that the point of the needle is really under the skin, and is freely movable while the injection is being made. On the whole the evidence regarding severe local complications does not justify refusal to employ either method in suitable circumstances, but it indicates the necessity of correct technique and the advisability of resorting to oral administration as soon as the condition of the patient permits.

(8) In the treatment of all cases of fever it should be remembered that it is quite wrong to continue giving large doses of quinine daily for many days if it is not obvious that the drug is doing good. Quinine is essentially a drug which, if it is going to do good at all, does so quickly. Hospital records in most tropical countries contain numerous examples of patients having received 30 or 40 grains of quinine daily for a month or more without any appreciable effect on the temperature: in all probability the disease from which these patients were suffering was not malaria, and in any case, whether they were suffering from malaria or not, it is certain that the quinine should have been stopped after the first week and the effect observed.

(9) Whether we are treating a primary attack or a relapse it is seldom or never necessary or advantageous to continue large doses of quinine (30 grains in 24 hours) longer than five days. At the end of that period the quinine treatment should be changed to one or other of the following plans of so-called "after-treatment" which should be carried on for three months:—

(a) *10 grains of quinine once daily.*

If this plan is adopted the daily dose should be begun on completing the treatment of the attack. It is most important that the time at which the dose is taken should be an hour or two before the time of onset of the febrile paroxysms in the attack or relapse which preceded the treatment.

(b) *30 grains of quinine on each of two consecutive days, e.g., Saturday and Sunday, each week.*

In this plan it is best to begin the treatment on the first Saturday after the cure of the attack. The amount should be taken preferably in four doses, the first at sunrise, the second at midday, the third at sundown, and the fourth at midnight.

(c) *30 grains of quinine on only one day each week, e.g., Sunday.*

The amount is best taken in four doses as above, but if the patient knows the usual time of onset of his febrile paroxysms he may be advised to take 15 grains an hour or two before that time and 15 grains six hours later.

(d) *15 grains of quinine on each of two consecutive days, e.g., Saturday and Sunday, each week.*

This plan is applicable to mild double tertian infections. The amount should be taken in one dose. The method has given very successful results when carried out in an efficient manner among British troops in India.

(*e*) 15 *grains of quinine on only one day each week, e.g., Sunday.*

This is applicable to patients in whom the primary attack was mild and quickly cured. The amount should be taken in one dose an hour or two before the time of onset of the febrile paroxysms in the patient's preceding attack or relapse. The method is commonly employed with great success in the jails of India.

A medical man who can overcome the all-important difficulty of ensuring that the particular routine selected will be conscientiously followed, will be able to obtain successful results with any of these methods of "after-treatment." In making a choice between them this difficulty should be the subject of first consideration.[1] Thereafter consideration should be given to the type and severity of the case and to a knowledge of the circumstances in which it was contracted. A plan which is sufficient to protect against relapses of a single infection contracted during a period of normal endemic incidence may be ineffective for a type which is the result of repeated infections contracted during a severe epidemic. It should be realised, too, that none of the above methods is designed to protect against *new infections.* The correct method of using quinine for this purpose will be described in Chapter IX; when a malaria patient has to remain in the malarious locality we must employ it *in addition to the selected plan for protecting against relapses.*

It may be added in connection with these and many other points (e.g., the time of day at which the dose is taken) that we cannot expect successful results unless we are prepared to devote great attention to detail—indeed we must insist that quinine treatment for protection against relapses should be carried out with the precision and technique necessary for a scientific experiment. The successful results obtained when this rule is followed are such as to justify a very critical examination of any reported failure.

Another very important rule in "after-treatment" is that whenever, in spite of following one or other of the routine plans, the patient has a relapse of fever, or whenever, even without a relapse, malaria parasites are found in his blood, he must go to bed and go through first the five-day course of treatment, and thereafter the selected course of "after-treatment" for three months, just as though his relapse had been a first attack. It is usually advisable, also, to revise the arrangements for ensuring that the selected plan is conscientiously followed.

(10) For the treatment of children we must give larger doses of quinine than are proportional to their body weight as compared with adults. They stand the drug

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[1] Judging by reports the difficulty was not often appreciated during the war.

well and it must be pushed as soon as the diagnosis has been established. For babies and small children *euquinine*, which is almost tasteless, should be used. It is weaker than quinine and the doses should be half as much again as those of the sulphate or hydrochloride. It must be given as the powder; if dissolved, the bitter taste returns. For a baby of one year it is suitable to give doses of 1½ grains of euquinine every six hours, and for a child of two years 3 grains every six hours. For children from three to five years doses of 5 grains of euquinine every six hours are suitable, and from five to ten years 7 grains (or 5 of the sulphate or hydrochloride). Although most children of ten years can stand 10 grains of the sulphate or hydrochloride of quinine taken in a single dose without being greatly affected by symptoms of cinchonism, it is preferable not to go beyond 5 grains at a single dose. To a child of ten this dose may be given every four hours without harmful effects.

In children it is particularly advisable to watch closely the effect of the quinine upon the temperature and the parasites, and to use these observations as a guide to dosage, especially with a view to stopping large doses of quinine as soon as the blood becomes free from parasites.

(11) Except quinine no drug has yet been proved to have a specific action on the malaria parasites, and careful experiment has confirmed the view that various preparations of arsenic are not efficient substitutes for that remedy. Arsenic, however, in small doses combined with iron is a useful *accessory treatment* during the apyrexial intervals between attacks. During these intervals it is most important to improve the patient's general health as quickly as possible. Quick improvement seldom occurs when patients remain long in hospital after an attack. As a general rule the best results are obtained when arrangements can be made for patients who are undergoing a course of "after-treatment" to pursue an open-air occupation in which their bodies and minds are fully occupied. During the earlier years of the war it was difficult to make arrangements for utilizing this well-recognized experience, but later the arrangements made in France for the systematic treatment and supervision of malarious patients who continued to perform their duties in the field, yielded excellent results. It is worthy of note, too, that in some obstinately relapsing cases, demobilisation, with return to the mode of life to which the patient was accustomed before the war, produced almost at once a remarkable improvement in general health, and a rapidly decreasing tendency of the illness to relapse. From this and many other experiences, we learn that protection against relapses is only partly a matter of the particular plan of quinine administration which may be advised.

(12) Finally we may note that the logical basis of quinine treatment for protecting against relapses is very simple: the measure, in whatever mode it is used, is merely an endeavour to attack the parasites as soon as they appear in the circulating blood

and before they have had time to multiply sufficiently to cause clinical manifestations. If it is admitted that quinine is *the* remedy when parasites are so numerous that they cause symptoms, it is reasonable to suppose that it will be equally effective when their number is not quite sufficient to do so. When we advise a patient to take 10 grains of quinine daily we realise that during perhaps six days of the week there are no parasites in the circulating blood on which the dose can act. But because we cannot state the exact day on which the parasites will appear in the circulation a daily dose is necessary to ensure that they will meet some quinine when they do so. From a knowledge of the time at which the patient usually has his febrile paroxysms we try to time this dose so that it will be most effective. (Most patients know, at any rate, whether their paroxysms usually come in the morning or in the evening.) The daily dose is a plan for attacking the parasites on their first appearance, which means at a time when even 10 grains is sufficient to drive them out of the circulation again. When we advise a weekly dose we realise that we are taking greater chances, but we try to counteract this by making the dose larger. We know that if the dose, say of 30 grains, is advised to be taken every Sunday, the parasites may have begun to appear in the circulation perhaps on the previous Friday—but we hope that the curative treatment on Sunday may be sufficient to destroy them before they have multiplied to the number at which they begin to cause clinical manifestations.

CHAPTER IX.

"Prevention" and "Eradication."

SECTION I.

In summarising the various methods which have been recommended for dealing with malaria it is well, in the first place, to separate those that aim primarily at *protecting against the disease* from those that aim primarily at *reducing* (*or extirpating or eradicating*) *the disease.*

In a policy of special sanitation the measures in the first category would be defined as "measures of defence," while those in the second would be defined as "measures of attack."

Next, for the purposes of summary, it is useful to note that while the arrangements for a policy of protection differ from those for a policy of reduction or eradication, both plans include certain methods in which quinine is used, and certain methods in which quinine is not used.

On the basis of these headings and sub-headings the different methods for dealing with malaria may be tabulated as follows:—

TO PROTECT AGAINST MALARIA

use
measures of defence
which may be

Methods in which quinine is used, namely,

(1) For protection against new attacks.
(2) For protection against relapses.

Methods in which quinine is not used, namely,

(3) Protection from the bites of mosquitoes.
(4) The segregation of the healthy.

TO ERADICATE MALARIA

use
measures of attack
which may be

Methods in which quinine is used, namely,

(5) The discovery and treatment of all human cases and carriers.

Methods in which quinine is not used, namely,

(6) The elimination of all malaria-carrying mosquitoes.

We see from this statement that there are six methods of dealing with malaria to be considered, of which four are used principally in campaigns of protection (usually called "prevention") and two in campaigns of reduction or eradication.

In this account it is proposed first to explain each of the methods as briefly as possible, then to state which methods are most suitable in certain circumstances, and, finally, to describe the manner in which, in practice, each method should be carried out.

(1) PROTECTION FROM THE EFFECTS OF NEW INFECTIONS BY TAKING QUININE (so-called "Quinine Prophylaxis").

Long before it was discovered how malaria is contracted and spread, it was known on empirical grounds that quinine swallowed regularly in sufficient doses is very nearly a complete protection against the clinical manifestations of malarial fever. Knowledge obtained subsequently supported this old experience, but other methods of protection became available, and at present quinine prophylaxis (for protecting against new infections) is used only as a last resort when more effective measures cannot be applied.

The correct method of using quinine for protection against new attacks is based on the following grounds:—

(*a*) We know, of course, that taking quinine does not prevent an infected mosquito from injecting the malarial sporozoites into the person whom it bites; therefore, taking quinine does not prevent malarial infection—what it does is to destroy the infection after it has been introduced into the body. (*b*) Quinine acts more effectively against the young forms of the malaria parasite than against the mature forms, and a very small quantity, if present in the circulation when the youngest forms (namely, the sporozoites), are injected by a mosquito suffices to kill them. (*c*) Therefore the way to prevent a new infection from having effect is to ensure that a little quinine will be in the blood at the time when one expects to be bitten by an infected mosquito. (*d*) Anopheles mosquitoes are active between sunset and sunrise, but their efforts to bite human beings are especially persistent just after dusk, and again just before dawn; these, therefore, are the times during which it is best to have quinine circulating in the blood. (*e*) Quinine taken by the mouth very quickly enters the circulation, but, unfortunately, very quickly leaves it, and it is doubtful whether any portion of a dose taken, say at 6 p.m., would be effective against sporozoites injected at 2 a.m., by which time all the quinine might have left the circulation. (*f*) Therefore, when protection is required during the evening and throughout the night, it is necessary to take a small dose of quinine about an hour before sunset, and a second dose about the middle of the night.

On these considerations, the best rule for protecting against new attacks by quinine is:—

Take a dose of 5 grains of quinine in solution every evening about an hour before sunset, and a second dose of 5 grains about midnight.

When people sleep under good mosquito curtains, the second dose is not necessary, because such people require protection only until they go to bed.

A dose of quinine taken in the morning is too late to destroy the sporozoites which were injected during the previous evening and too early to destroy those which will be injected during the coming night.

(2) PROTECTION AGAINST RELAPSES BY TAKING QUININE.

This subject has already been considered in sufficient detail on p. 188. It is often a hard task to remove the confusion which exists in the minds of many people as to the difference between methods of using quinine for protecting against relapses, and for protecting against new infections, but when the task can be accomplished the results justify the labour. Relapses are not caused by the bites of mosquitoes.

(3) PREVENTION BY PROTECTION AGAINST THE BITES OF MOSQUITOES.

The plan of attempting to protect everyone in malarious districts from the bites of infected Anopheline mosquitoes by the strict use of mosquito nets for individuals, and by mosquito-proofing or "screening" houses with wire netting, was first advocated on a large scale by Professor Celli in Italy. The rules to be followed by individuals, and the manner in which houses, wards, &c., should be screened, will be described in Section II of this chapter.

(4) PREVENTION BY THE METHOD KNOWN AS THE SEGREGATION OF THE HEALTHY.

This plan was initiated by Drs. Stephens and Christophers for the protection of Europeans in Africa. It advocates that people who have never had malaria, but are obliged to live in a malarious district, should live at least half a mile away from the village or town containing the local inhabitants among whom malaria is endemic, and who are the chief source from which Anopheline mosquitoes become infected. The method should always be adopted by travellers and by regiments when marching through a malarious district, and should be taken into consideration when selecting sites for huts or permanent buildings wherever malaria is endemic.

(5) ERADICATION BY THE DISCOVERY AND TREATMENT OF ALL HUMAN MALARIA CASES AND CARRIERS.

This measure of attack aims at the extermination of all malaria parasites by the systematic treatment of all infected individuals with quinine. Dr. Robert Koch, who obtained successful results by employing it in a number of malarious localities, likened it to the campaign against cholera; just as in cholera it is necessary to search out all the sick, the convalescent, and the healthy, who harbour the cholera vibrio, and to isolate and disinfect them, so in a campaign against malaria it is necessary to search out and disinfect all people who harbour the malaria parasite. The quinine treatment of all human malaria-carriers prevents Anopheline mosquitoes from becoming infected, so that after a time the disease dies out.

(6) ERADICATION BY THE ELIMINATION OF ALL MALARIA-CARRYING MOSQUITOES.

The plan of attempting to extirminate or to reduce the number of Anopheline mosquitoes in malarious districts was initiated by Sir Ronald Ross, the discoverer of the facts upon which modern systems of prevention and eradication are based. The measures necessary for the control of mosquitoes in general, and for the suppression of Anopheline mosquitoes in particular, will be described in Chapter X.

APPLICABILITY OF THE DIFFERENT METHODS.

Having thus briefly defined the various methods recommended for dealing with malaria, we may now endeavour to ascertain the circumstances to which each of them is particularly applicable. This may best be done by considering the problem from the points of view of:—

(*a*) The individual.

(*b*) A particular body of individuals such as a regiment of soldiers or the inmates of an institution.

(*c*) Communities.

The individual who has to live in a malarious place must think first how best he can protect himself against contracting the disease. There is no doubt that any individual who is in a position to do so may effectually protect himself from becoming infected, by taking measures to prevent himself from being bitten by mosquitoes. This has been proved, and at present is not doubted by anyone who is capable of forming an impartial opinion on the subject. The three rules of personal protection against being bitten will be described in Section II, and anyone who follows them carefully can live in the most malarious country with impunity. An additional safeguard for the individual, which no wise man would neglect is to utilize the prophylactic method known as the "Segregation of the healthy," by taking care not to sleep within half a mile of known human sources of infection. In malarious localities in the tropics the native children in villages are nearly always the chief source of infection.

If for some good reason an individual is not able to prevent himself from being bitten by Anopheline mosquitoes, nor to keep away from human sources of infection, he must fall back upon the plan of taking prophylactic doses of quinine every evening according to the method already described. It should be emphasized again, however, that the taking of quinine to prevent the clinical effects of new infections is only a last resort suitable for an emergency, but not necessary nor advisable when the rules for protecting against mosquito bites can be followed.

The plan of taking quinine which has been described for protecting against relapses is not the correct method of endeavouring to protect against the results of new infections.

The correct measures for limiting new infections among *a particular body of individuals* are usually similar to those just mentioned; we may have to disregard measures among the inhabitants of the place, and think only of the protection of the body of men in our charge. This is necessary, for example, when a regiment of soldiers is marching through, or is temporarily encamped in, a malarious district of an enemy country; and it is sometimes equally necessary, though perhaps less obvious, as regards more or less permanent hutments or barracks in malarious areas surrounded on all sides by villages and by breeding places of Anopheline mosquitoes. If malaria is endemic in the locality, the villages usually provide the human sources from which the Anopheline mosquitoes become infected, and if the huts or barracks are in the midst of the villages the soldiers will suffer severely from malaria. In such cases the protection of the men will often be attained more efficiently and cheaply, and with less inconvenience to all concerned, by adopting the principles already indicated for the individual than by any other plan.

Measures for Communities.—No policy can be considered entirely satisfactory that aims at the protection of only a few, however important these few may be, while it leaves the bulk of the inhabitants of a place in the same condition. In a community the object of measures should be to render *everyone* less liable to contract malaria—to transform, in fact, the malarious place into a healthy one. For this reason no system of "defence" alone can be regarded as sufficient for communities; we must adopt for them one or other of the methods of "eradication."

The choice as to which of the two methods of eradication to adopt will sometimes be difficult, but it is always advisable to make it, because, in dealing with malaria in a community, much more effective results are usually obtained by concentrating effort upon one well-planned method than by dispersing endeavour along several lines.

As regards eradication by the suppression of Anopheline mosquitoes, it must be stated that *in places which can justly be called malarious*, the task of reducing the number of these insects to a degree sufficient to lessen materially the prevalence of malaria is always very difficult. When the suppression of Anopheline mosquitoes was first recommended as a means of getting rid of malaria, it was thought that in nearly all malarious places the task would be comparatively easy and inexpensive. It was hoped, indeed, that it could be accomplished by a "new method," which consisted essentially in carrying out such small works of surface drainage, obliteration of pools, and "petrolage," as could be done by a few labourers banded together to form a body styled, later, a "Mosquito Brigade." This method was entirely different from the old method of reducing malaria by drainage of the soil, its chief advantages over that method being its great simplicity, its cheapness, and the fact that it inconvenienced the general population of a place only very slightly, if at all. On the assumption that this method would be successful, many campaigns were begun; but as they proceeded it was found that, although such minor measures are useful against the strictly local, so-called "domestic," species of mosquitoes, they have little or no effect on the number of Anophelines. When this was realized, it became obvious that the suppression of Anophelines is not a method of reducing malaria that can be adopted everywhere, and that before deciding to adopt it in a place we must ascertain whether, as Sir Ronald Ross has said, "the game is worth the candle."

In endeavouring to forecast whether efforts to reduce anophelines in a limited area are likely to be successful or not, the first step is to ascertain the condition of the drainage within the area and for some miles round it. If the drainage is so perfect that waterlogging of the soil does not occur, even in seasons of exceptional rainfall, it is very likely that measures to reduce anophelines will be successful, but if the drainage is imperfect the task will usually prove to be beyond the resources available. It is also very important to ascertain whether anophelines are breeding in swamps, &c., in the country surrounding the area; it has been proved that when this is the case the obliteration of breeding places locally within the area is useless.

It is the case, however, that the breeding places of a few species of anophelines are so specialised that, when it has been proved that one or other of these species is responsible for spreading malaria in a locality, a campaign against it is always the correct course to pursue. A notable example occurred in Bombay, where a severe outbreak of malaria was traced to *A. stephensi*, which was breeding exclusively in disused wells. *A. plumbeus* is another species with peculiar breeding places comparatively easy to deal with.

As regards reduction or eradication by the discovery and treatment of human cases and carriers, it may be said that, because this method aims at finding and treating vigorously everyone who is suffering from malaria in the locality concerned, its effect in stopping deaths from the disease and preventing serious illness and prolonged disability begins at once. It is therefore a direct method of attaining the object desired. In most malarious places in the tropics the immediate need is a plan for lowering the mortality and diminishing the enormous amount of suffering and loss of labour which is inevitable in the absence of adequate arrangements for the treatment of attacks. In India the annual deaths believed to be due to malaria exceed a million, and in the epidemic year of 1908, among the civil population of the United Provinces, one person in every twenty-four is said to have died from the disease. Knowing, as we do, that malaria, when properly treated, is by no means a fatal disease, it would seem to be a first duty in such countries to concentrate attention upon arrangements for the treatment of cases.

From the point of view of the indigenous inhabitants of the tropics it is unfortunate that arrangements for meeting this elementary need have been retarded partly by the belief that, because mosquitoes cause malaria, their elimination should be the object of chief concern and expenditure, partly by the knowledge that quinine, as usually taken for prophylactic purposes, does not afford complete protection against attacks. I think that, whatever views are held on these subjects, there should be no difference of opinion as to the paramount duty of bringing quinine within reach of all classes of people. Even in India millions of people are still unaware of the existence of a drug like quinine, and of those who know that there is such a drug, not a fractional proportion know where it can be obtained, or how to use it, or what great benefits its regular use would confer upon them.[1] On these considerations I think it is unfortunate when medical men discourage or criticize any effort or expenditure which administrative authorities may be willing to make for the widespread distribution of quinine. Sometimes it seems to be forgotten that quinine is freely distributed in the tropics not in the belief that it will entirely prevent people from contracting malaria, but in the knowledge that, if they do contract the disease, it will prevent their attack becoming so severe as to kill them or to render them so ill that they cannot work. It is for reasons of this kind that those who are actually in touch with the practical problem consider that the wide distribution of quinine is a public duty justifying heavy expenditure, and constantly urge the authorities in tropical countries to continue making the drug available to everyone.

In England mosquito surveys of the localities in which cases of indigenous malaria occurred during the war showed that in those areas it would be a task of great magnitude to reduce the anophelines to a degree which would prevent risk of the inhabitants being bitten. Moreover, the proceeding, if carried out on a sufficient scale in the areas concerned, would make demands on the supply of available labour and entail an amount of interference with agricultural work that could not justifiably be asked for during war time without much stronger evidence of its necessity than could then be put forward. In the low-lying marshy areas which were chiefly affected drainage is non-existent or bad, and, even if funds and labour and materials for carrying out a drainage scheme had been available, several years would have been occupied in doing the work. Considerations such as these made it necessary to forego, at least for the period of the war, the excellent opportunity which presented itself of attempting some exact experimental work on anopheline eradication under English conditions. But on general sanitary grounds it is greatly to be hoped that the time will soon be favourable for an experimental campaign on an adequate scale against these insects in this country. The lessons of such a campaign, if it were carried out and tested by modern methods, would be of great service not only to England but to the colonies and malarious countries everywhere.

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[1] Yet India has led the way to the world in general in taking steps for providing and distributing quinine. See a note by the author on "Some of the Measures taken to make Quinine available to the Poor in India," published in *Paludism*, No. 3, 1911.

Meanwhile in this country the measures based upon the discovery, treatment and supervision of cases and carriers have worked well in practice, and they are, of course, the only measures applicable to the present condition in which numerous relapsing cases of malaria are scattered singly, or in twos and threes, almost everywhere throughout the country. (See the map on p. 90.)

On theoretical considerations the best results in reducing or eradicating malaria ought to be obtained by employing *all available methods at the same time.* It seldom happens, however, that the resources of a community are sufficient for such a comprehensive campaign ; and the usual result of an attempt on these lines is that not one of the measures is brought to the degree of perfection at which it begins to have any effect on the incidence of malaria. The campaign in the Panama Canal zone was a brilliant exception to this general rule, but it is known that even in that campaign the wasted effort which resulted from unavoidable failure to bring certain of the measures to the "minimal effective degree of perfection" was enormous. In that campaign the men who were personally engaged in the work were never under a misapprehension on this subject,[1] but journalists and popular writers constantly failed to realize it. Logically it seems reasonable to suppose that even a little anti-mosquito work, or a little screening, or a little distributing of quinine must inevitably do *some* good, but, unfortunately, the results of practical work do not support this conclusion. Perhaps we must make allowances for the frailty of man as well as for the wiliness of the mosquito—but whether this is true or not, practical experience is to the effect that it is usually best to concentrate all available effort on one carefully selected method which can then be brought to a high degree of perfection.

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[1] See "Mosquito Control in Panama," by J. A. Le Prince and A. J. Orenstein (Putnam's, 1916).

CHAPTER IX (*continued*).

SECTION II.

PRACTICAL RULES FOR CARRYING OUT THE METHODS OF PREVENTION AND ERADICATION.

METHOD I.—QUININE FOR PROTECTING AGAINST NEW ATTACKS.

Rules for using quinine for this purpose and the grounds on which the method is based have already been given in sufficient detail.

METHOD II.—QUININE FOR PROTECTING AGAINST RELAPSES.

Medical officers who have had most experience in using quinine for this purpose hold the view that the results obtained among troops and other bodies of men are dependent almost entirely on the degree of supervision and control which can be exercised during the preparation and during the administration of the doses. The following is an account of a procedure devised by Major Heard, I.M.S., which yielded remarkably successful results in some Indian jails:—

The dose selected was 15 grains to be given in a single dose every Monday morning at the time when the prisoners were drawn up for the weekly parade. The articles used in connection with the measure were: (1) quinine sulphate in powder; (2) dilute sulphuric acid; (3) water; (4) a pair of scales and weights; (5) a large vessel or jar having a wide mouth provided with a lid which could be sealed up; (6) a long-handled wooden ladle holding exactly one ounce; (7) small glass tumblers, one for each person who was to take the prophylactic dose. These tumblers were obtained in the local bazaar and were of different colours; plain white ones were used for Hindus, green ones for Mohammedans, and brown ones for others.

Every Monday morning, at the time when the office work of the jail was being done, the compounder was required to bring the quinine, the acid, the water, the scales and the large jar into the office. The calculation of the amount of quinine which would be necessary for the number of men on parade, the weighing out of the quinine, the addition of water and acid in such amount that one ounce of the mixture would be a dose, and the transference of the mixture to the large jar were then carried out under the medical officer's supervision. Then the lid of the jar was sealed. At the parade, which was held just before the morning meal, the tumblers were distributed and the jar opened. The men were divided into small parties or squads, and at a word of command each man in the squad held his tumbler at arm's length in front of him. The vessel containing the mixture being carried by one man and the long-handled ladle by another, the medical officer and these men then passed down the line, a dose of mixture being ladled out into each man's glass on the way. Each man in the squad was required to keep his tumbler at arm's length until the distribution of the doses to all men in the squad was completed. Then at a word of command all drank the dose, and immediately afterwards the medical officer passed along the line again for the purpose of examining each man's teeth and gums (for signs of scurvy, &c.) and of ascertaining that the dose had been swallowed.

The "Second Report on the Anti-malarial Operations at Mian Mir. 1901-1903," contains some good examples of the protective effect of quinine when administered with scientific accuracy to British troops, and of the futility of the measure when the drug is given without supervision or under regimental supervision. The dose selected was 15 grains on two consecutive days weekly. The experiments were carried out by Major Christophers, I.M.S. In a first experiment among 100 men who volunteered to swallow the doses regularly the admission rate for malaria was 20 per 1,000, as compared with a rate of 200 per 1,000 during the same period among men not taking the drug. The measure was then made compulsory for large bodies of men, a nominal roll of each company being kept on which each dose taken was entered. The men were paraded and the administration was carried out under a medical officer's supervision. The administration was thoroughly done, but it was difficult to be sure that men who were absent from the parade on various duties received their dose of quinine on returning to barracks. The results were not so good as in the first experiment, but the accompanying chart of weekly admissions for malaria showed that they were quite definite. Experiments were then made of giving quinine under regimental supervision. It was found that in every experiment of this kind not the slightest effect was evident. It appeared that under this plan of administration it was quite impossible to maintain adequate supervision even when the administration was supervised by a regimental officer, and it was quite uncertain how many men received quinine regularly.

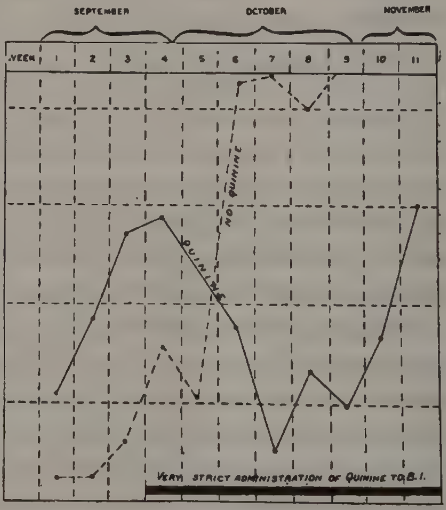

FIG. 92.

The general conclusions drawn from the experiments were that when very stringent regulations can be brought to bear upon carrying out the measure it is a most effective means of lowering the fever rate among troops, but that without this stringency the measure is of little or no value.

METHOD III.—PROTECTION FROM THE BITES OF MOSQUITOES.

Rules for the Individual.

Rule 1.—Never go to sleep except under a good mosquito curtain.

Rule 2.—After sunset always wear sufficient clothes to protect the whole body from mosquito bites.

Rule 3.—In addition, when your environment or occupation is such that you cannot, by active movement, prevent mosquitoes from biting your face and hands, wear a gauze net to protect the head, face and neck (fig. 93), and gloves to protect the hands and wrists.

The following details are important:—

Note to Rule 1.—The rule must be applied always; not only during the night.

Beds should be broad and long, so as to leave a good space between the sleeper and the mosquito net. The net should be rectangular and not less than 16 meshes to the inch. The net should be hung inside the poles, and the sides and ends should not trail on the ground, but be tucked under the mattress. If there are no poles the curtain can be arranged properly over the bed by hanging it with string from nails at each corner of the room. If a bed is so small that the sleeper's feet, or parts of his body, touch the net, a strip of cloth should be sewn round the net just above the level of the mattress, so that mosquitoes resting on the outside of the net cannot bite the sleeper through the meshes. The net should be stretched tightly so that air may pass freely through it. After getting into bed the inside of the net should be carefully examined for mosquitoes.

Note to Rule 2.—Many cases of malaria are contracted when men are sitting about in shirt-sleeves and "shorts" after the day's work is over; others during dinner when people wear thin socks and low shoes. In a malarious place during the evening high boots or putties should be worn inside a thick pair of trousers, and always a coat. Beware of openwork cane-seated chairs.

Note to Rule 3.—In very malarious localities, and especially in localities infected with yellow fever, watchfulness and active movement are very necessary. In such places it is a good plan to go about with a friend, or servant, who can quickly brush off any mosquito that has alighted on the neck or face. In malaria-infected huts an easy way of catching anophelines is to sit motionless with hands outstretched over a table, and to get an assistant to catch the anophelines in test-tubes as they alight on the hands. If you have no gauze net for the head and face, rub oil of citronella on the neck and back of the ears.

It is necessary to be particularly careful to avoid being bitten by mosquitoes when visiting outposts and villages or making excursions into localities in which most of the native inhabitants are infected. The Health Department of the Panama Canal Zone recently recorded the following instances of malaria contracted during visits of this kind. Three boy scouts who were on a camping trip down the Chagres River were bitten by mosquitoes each night. Several ladies from Ancon went on an excursion to the Sabanas and Bella Vista, remaining until late in the evening; an employee went on a hunting trip to Arraijan, and another had been fishing at Pearl Island, remaining there the night. All of these people, within a fortnight after their return to Ancon, began to suffer from malaria. Similar instances are commonly recorded in India.

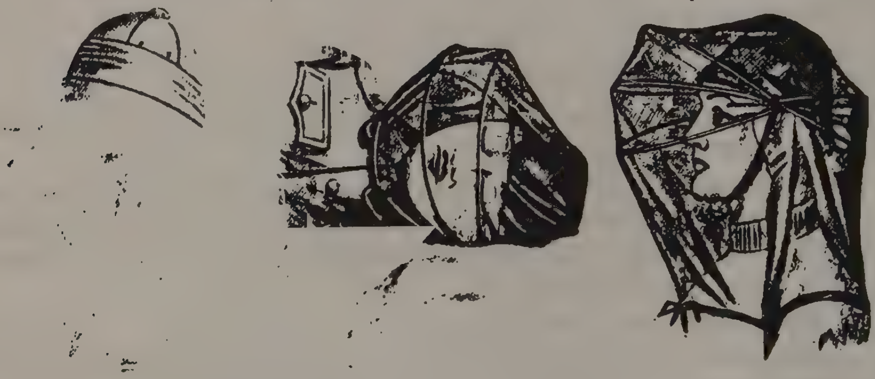

FIG. 93.—The "Simpsonette" patent protective headgear.

Rules for Huts, Wards and Houses.

Space does not permit an adequate description of the method of mosquito-proofing or "screening"—for in this matter, as in quinine prophylaxis and mosquito control, the secret of success is minute attention to detail and the adoption, from the beginning, of the best system available. The most important principle to be followed is to carry the screening broadly round the hut—along the verandah posts or on a special framework—rather than to attempt to overcome, one by one, the numerous small problems that arise during the separate screening of each window, door, ventilation aperture, crevice and crack. A properly screened hut is really the original hut within a larger screened chamber to which there is only one means of entry and exit, namely, a porch with double doors, both opening outwards, but hung from opposite sides. This principle was evolved and carried out with great thoroughness in Ancon and some other chief stations along the Panama Canal. The illustration in fig. 94, taken from a photograph published in "Mosquito Control in Panama," by Le Prince and Orenstein, indicates the principle better than a written description.

A hut or ward that is screened imperfectly, even when only one or two apertures have been overlooked, is often more dangerous than an unscreened hut, because a few mosquitoes will probably succeed in entering it, and (not easily finding an exit) will remain in it long enough to infect every new occupant.

FIG. 94.—Screened houses on the Panama Canal.

The wire netting used for screening should be non-corrosive, and it is a good practice to have it blackleaded and brushed once a month so as to prevent the meshes from becoming clogged with dirt. The grade should be 16 meshes to the inch. Doors that men are likely to open by pressing their hands against the wire should be protected by a layer of strong hen-coop netting fixed over the wire gauze.

Save as an admitted measure of emergency, attempts to screen huts by nailing butter-muslin over the windows and other apertures should be deprecated; the result is usually to convert the hut into a mosquito-trap, and in the long run the expense and labour required is often as great as if the matter had been dealt with properly from the beginning. If it is adopted, muslin-screening must be examined daily to detect and repair all gaps, tears, and holes.

Men occupying screened huts should be taught how to enter the hut without introducing mosquitoes at the same time, and they should go in and out as little as possible. The door of a screened hut on the Panama Canal was watched between 5 and 8 o'clock one evening; it was found that the frequent entry and exit of the occupants caused the door to be open a third of the time.

In huts and wards (whether screened or not) daily hand-catching of mosquitoes is essential.[1]

If screening cannot be carried out according to the principles noted above, it is preferable to give each individual a good mosquito curtain *and to see that he uses it correctly.*

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[1] We have found that the occupants of "malarious houses" in England readily adopt this measure when its purpose is explained to them.

An Example of an Unsatisfactory Type of House in a Malarious Locality in the Tropics.

The accompanying photograph (fig. 95) of a house intended for a European on a State railway in an exceedingly malarious locality in the tropics is worthy of study. Some of the faults of this house are: (*a*) absence of projecting eaves and verandah on the side that is exposed to the full force of the tropical sun; (*b*) the roof is a single layer of rather thin flat tiles, and there is no ceiling; in the absence of a substantial wood ceiling, a single layer of flat tiles is an inadequate protection against the sun; (*c*) the windows are very small in proportion to the floor area; it is generally agreed that for houses in the tropics the window area should be at least one-fourth of the floor area; (*d*) absence of windows and doors in the side wall on the ground floor; there is no through ventilation on this floor; (*e*) no provision for mosquito-proofing, and a type of house in which this essential measure would be difficult to apply; (*f*) a type of house that is almost unbearably hot and does not provide the minimum comfort necessary for the health of Europeans in the tropics.

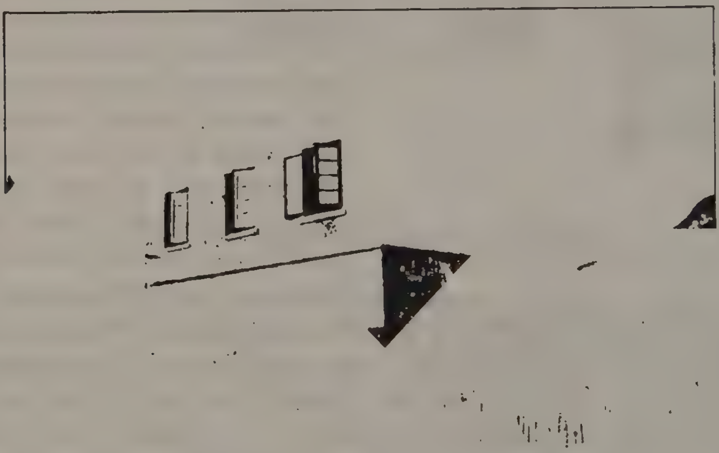

FIG. 95.—An unsatisfactory type of house for a malarious locality in the tropics.

The Type of House that is desirable.

In malarious places in the tropics the objects to be aimed at are that the houses should be as airy as possible, as cool as possible, as shaded as possible, and that they should be entirely protected against the entry of mosquitoes. In addition they must be sufficiently substantial not to be affected by the very strong winds and heavy rain

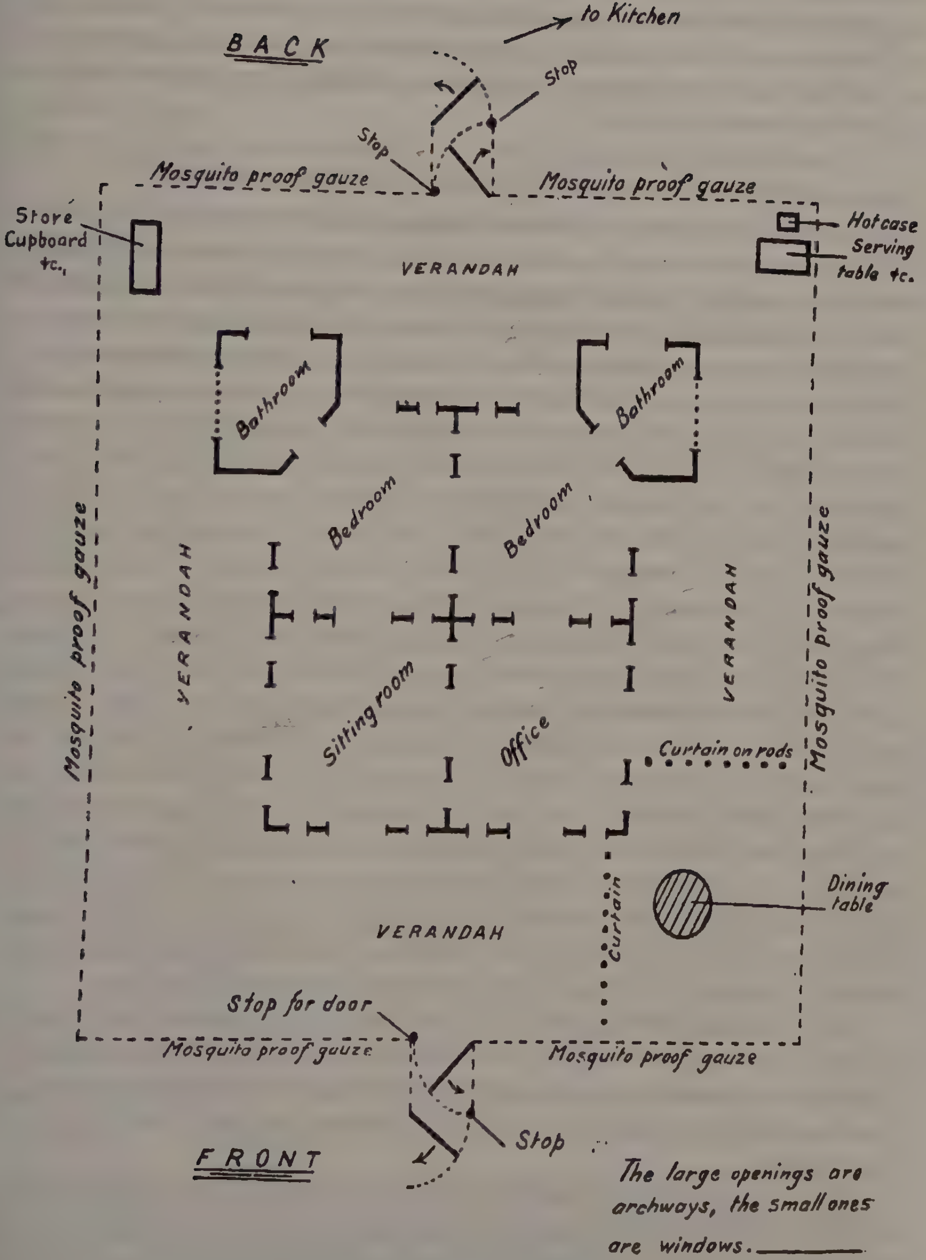

FIG. 96.—Sketch plan of a suitable house.

of the monsoon and must be proof against the attacks of white ants. The following are some principles which are recognized as being useful for attaining those objects.

(1) As a rule the houses should be square, and may be of one or two storeys.

(2) They should be raised from the ground, preferably on an extensive plinth of concrete, surfaced with cement.

(3) The whole area of the plinth should be utilized for the erection of a large "mosquito-proof shed" inside which the house proper will be built.

(4) The "shed" consists of the following parts: (*a*) Pillars or uprights of iron, stone or wood erected at the corners and along the outer limits of the plinth to support the roof; (*b*) between the pillars a dwarf wall and upon it a framework filled in with mosquito-proof copper wire gauze of 16 (or preferably 18) meshes to the inch; (*c*) at one or at most two places in the skeleton walls double doors, mosquito-proofed, and both opening outwards; they should be made to close automatically. (N.B. It is essential to the success of mosquito-proofed houses that all doors should open outwards); (*d*) a ceiling of wood or of asbestos material, resting on and closely applied to the top framework and girders in such a manner that the attic is completely shut off from the remainder of the shed; (*e*) a sun-proof and rain-proof roof which is ventilated and of which the eaves project as far as possible beyond the framework and are not provided with gutters—the rain dripping from them being allowed to fall into a concrete drain laid all round the house; (*f*) the result is a large, square, mosquito-proof structure with walls of mosquito-proof wire gauze, a ceiling of wood, a floor of cement, and the whole covered by a roof; (*g*) all that now remains to be done is to reserve a broad space all round inside the structure to serve as a verandah and then to partition off the remaining space into rooms. The partitions need not be very substantial structures and they should be opened wherever possible by large arches and windows; doors to the arches are not necessary. It is important that no partition should stop a through draft of air from front to back and side to side of the house; (*h*) the house should be orientated so as to obtain the best advantage from winds; (*i*) the kitchen and servants' quarters must be in a separate little building away from the house.

The sketch facing this page (fig. 96) illustrates the above rules for what might be called a "four-roomed house," but it is the case that in houses of this type not many "rooms" are necessary, because a portion of the verandah is always used as a dining-room and another portion may be used as a bedroom; and this is the correct and healthful plan.

In connection with the observations on "malarious houses" recorded on pp. 68, 88 and 93 it should be noted that a good deal can be done to lessen the risk of being bitten, by giving attention to details of construction and furnishing of living rooms and bedrooms. A well-ventilated white-washed room which is free from superfluous cupboards, draperies, books and pictures is obviously less likely to harbour anophelines than a dark, dust-laden room. In some malarious stations in India there are European houses which have acquired such a malarious reputation that none of the older residents will live in them. Their design is such that they act as "mosquito traps."

METHOD IV.—PREVENTION BY SEGREGATION OF THE HEALTHY.

In many malarious districts the season of new infections lasts for only about three months, during which it is practicable for soldiers to camp out in tents on a place which, while being sufficiently near their area of duty, is sufficiently far from all human sources of infection to ensure their freedom from malaria.

The following sketch (fig. 97) illustrates a condition commonly met with in Indian cantonments.

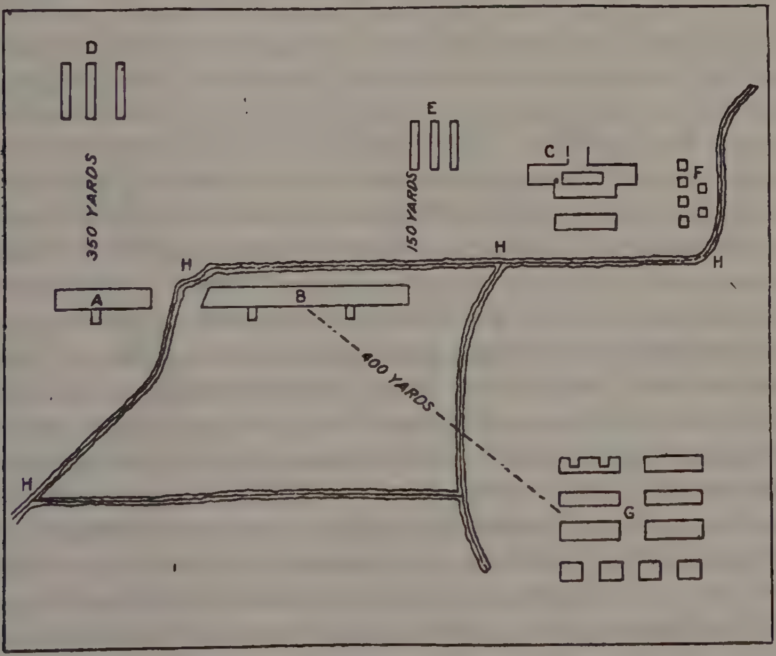

FIG. 97.

A and B are the barracks of the European troops. C is the hospital and military prison. D and E are the native followers' quarters containing perhaps 200 native children from 40 to 60 per cent. of whom have malaria parasites in their blood. F. is the hospital followers' quarters containing 40 or 50 children, 60 per cent. of whom have malaria parasites in their blood. G is the regimental bazaar containing numerous children, most of them infected. All these native children form a constant and abundant source from which the numerous anopheline mosquitoes which breed in the irrigation watercourse (H H H) become infected. It will be obvious that under these conditions the men in the barracks must suffer severely from malaria; they are in the midst of an area of infected anophelines and unless very stringent precautions to guard again mosquito bites were taken it could only be by a fortunate chance that any man would escape the disease.

In the locality from which this example is taken the season of new infections lasts only three months, and no explanation is necessary to make it plain that, in the particular instance cited, the simplest, cheapest, and most satisfactory method of prevention would be for the soldiers to camp out in tents during that season on a site where they would be a safe distance from the dangerous area.

METHOD V.—THE DISCOVERY AND TREATMENT OF CASES AND CARRIERS.

In the tropics it is seldom possible to carry out this method in a thorough manner except in certain more or less isolated communities of people who are either under control or are sufficiently educated to understand and voluntarily adopt measures designed for their advantage. Nevertheless it is a first duty to attempt the method *at least to the extent of providing every facility for the proper care and treatment of those who desire to avail themselves of it.* The establishment of hospitals, out-patient dispensaries, and arrangements for popularizing the use of quinine and bringing it within easy reach of the people are important items to consider, as well as systems of free distribution of the drug and education in the manner of its use. In some malarious districts in the tropics much good has been done by "travelling dispensaries" and "demonstration camps," which remain some weeks in the affected areas treating cases gratuitously, issuing free supplies of quinine, and explaining to the people how they can help themselves to get rid of the disease.

In its complete form the method of eradication by discovering and dealing with all cases and carriers is particularly applicable to a country like England in which compulsory notification of cases can be introduced and can be supplemented by house-to-house inquiries and the taking of blood films on a large scale. For this reason the general administrative lines of action adopted for dealing with malaria in this country are based essentially on this method of eradication, the details being embodied in THE PUBLIC HEALTH (MALARIA, &c.) REGULATIONS 1919 issued by the Local Government Board (now the Ministry of Health). The following are relevant extracts from these regulations.

Article II.—These Regulations shall come into operation on the First day of March, One thousand nine hundred and nineteen, and shall then and thereafter apply and have effect throughout England and Wales, and shall be enforced and executed by every Local Authority.

DUTIES OF MEDICAL PRACTITIONERS.

Article V.—* * * Every Medical Practitioner, as soon as he becomes aware that a person upon whom he is in professional attendance is suffering from malaria, * * * shall forthwith make and sign and send or deliver to the Medical Officer of Health a notification of the case in the form and containing the particulars set forth in Schedule A or Schedule B as the case may be, of the Public Health (Notification of Infectious Disease) Regulations, 1918, and shall transmit the notification to the Medical Officer of Health for the District.

Provided that a Medical Practitioner should not be required to notify a case of Malaria, * * * under this Article and shall not be paid a fee for so doing if the case has already, to his knowledge, been notified under these Regulations or under the Infectious Disease (Notification) Act, 1889, within the period of six months immediately preceding the date on which he first becomes aware of the disease in that case.

DUTIES OF MEDICAL OFFICERS OF HEALTH.

Article VI.—A Medical Officer of Health on receipt of a notification under these Regulations in relation to a case occurring in a place which is not in his District shall forthwith notify the Medical Officer of Health of the District in which the place is situated.

Article VII.—Upon the receipt of a notification under these Regulations, or on becoming aware in any other way of a case or suspected case of Malaria, * * * in his District, the Medical Officer of Health, or an Officer of the Local Authority acting under the instructions of the Medical Officer of Health, shall make such inquiries and take such steps as are necessary or desirable for investigating the source of infection, for preventing the spread of infection, and for removing conditions favourable to infection, and if a Medical Practitioner is not in attendance on the patient, the Medical Officer of Health shall also take such steps as are necessary or desirable for ascertaining the nature of the case.

Article VIII.—The Medical Officer of Health, on becoming aware of the occurrence within his District of—

(*a*) * * *

(*b*) a case of malaria in which he has reason to believe that the infection was contracted in the United Kingdom, shall immediately send to Us (the Ministry of Health) the name and address of the patient.

* * *

Article IX.—In every case of Malaria, * * * in his District of which he becomes aware, the Medical Officer of Health shall take such steps as appear to him to be necessary and practicable, to secure the treatment of the case in a suitable hospital, unless he is satisfied that treatment elsewhere than in a hospital will be carried out with all such precautions as are necessary to prevent the spread of the disease.

Article X.—In every case of malaria occurring in his District of which the Medical Officer of Health becomes aware, *and in which he considers that action is necessary to prevent the spread of infection,* he shall take all practical steps to ensure that the person suffering from malaria—

(1) Is supplied with efficient mosquito netting.
(2) Receives necessary quinine treatment,
(3) Receives proper advice as to the continuation of quinine treatment in order to prevent relapses, and
(4) Receives proper advice as to the precautions to be taken to prevent the spread of infection.

Article XI.—On the occurrence within a District of two or more cases of malaria *in which the infection has, in the opinion of the Medical Officer of Health, been contracted within the District,* the Local Authority may and if required by Us shall appoint and pay a Medical Practitioner approved by Us, who shall :—

(1) Make systematic visits to houses where Malaria has occurred or where risk of malaria infection arises, and shall offer to examine persons therein who are suspected of being infected with malaria, and shall endeavour to obtain material for microscopic examination in order to determine whether malarial infection is present, and
(2) secure that effective measures are taken to prevent the spread of infection by the administration of quinine, by the use of mosquito netting, and by the destruction of mosquitoes and otherwise.

METHOD VI.—ERADICATION BY THE ELIMINATION OF ANOPHELINES.

The methods of carrying out a campaign with this object will be described in Chapter X.

The opportunity may now be taken to state briefly the lines of action which were recommended as a result of the malaria survey in a tropical area which was described on pp. 98 to 107.

The problem has to be considered in relation to :—

(*a*) The temporary labour force engaged in constructing the railway and buildings

(*b*) The permanent staff who would reside at the port when the station was open to traffic.

(*c*) The conversion of the locality into a comparatively healthy one.

As regards the temporary labour force, suggestions were made under the following headings :—

(1) *Vital statistics.*—A record of the vital statistics of the labour force should be collected and compiled at regular intervals, so that the chief results, such as the age and sex composition of the force, the sickness and mortality rates, the invaliding rates, and the chief causes of sickness, death and invaliding, would be readily available at any time.

(2) *Selection of coolie labour.*—It might be possible to exercise selection of the coolies employed so as almost to eliminate the factors of non-immune immigration, and to weed out all "chronic malaria carriers."

(3) *Social and economic protective measures.*—Suggestions were made relating to food and wages, water supply, housing, arrangements for personal cleanliness, the provision of latrines and other matters of general sanitation. It was recommended that all borrow pits should be filled in, not so much for the reason that they were prolific breeding places of mosquitoes, as that they were a means of spreading cholera, dysentery and other intestinal diseases; for it was found that the same borrow pit was used by some coolies as a source of drinking water, by others as a latrine, and by others as a bathing place.

(4) *Regular medical inspection of the labour force* was suggested at least every fortnight, to be supplemented by visits to the quarters of those who were absent through sickness. It was suggested that the blood of everyone should be examined at intervals of six weeks.

(5) *Sanitary inspection of the lines* was suggested as a weekly routine.

(6) *Treatment of the sick.*—The arrangements were unsatisfactory because, as a general rule, sick coolies had to walk two miles to a Government Dispensary for treatment. It was suggested that the labour camp should be self-contained as regards its medical and sanitary arrangements, a temporary hospital and out-patient clinic being erected and the whole-time services of a medical officer being obtained. It was considered that this measure alone would certainly effect a great amelioration of the effects of malaria.

(7) As regards the permanent staff, additional suggestions were made relating to the desirability of following as far as possible the principles of the plan for the "segregation of the healthy" in selecting sites for permanent buildings and in making such buildings of suitable type and mosquito-proof. The removal of certain small native hamlets which were important sources of infection was also suggested as being desirable.

(8) The problem of how best to convert the locality into a healthy one required further study not only in the area immediately concerned but in the district as a whole. Attention was drawn to the influence of rainfall on malaria and it was stated that measures which failed to take the factor of floods into account would not be likely to bring about a definite reduction of the disease. If that were true, the problem would be an engineering one for devising an effective means to prevent flooding. Owing to the flatness of the country and the high level of the subsoil water, the problem was difficult, and perhaps its only solution would be the raising of the whole area several feet by extensive "hydraulic fill" operations. It was pointed out that the common assumption that the borrow pits were the chief cause of the prevalence of malaria was disproved by the knowledge of the conditions in similar villages where no borrow pits were present. On other grounds, however, the obliteration of the borrow pits was a necessary measure, and this work should not await the solution of the larger problem. It was suggested also that as a measure of general sanitation the cost of a small staff of inspectors and labourers for the chief purpose of finding and dealing with mosquito breeding places and with insanitary conditions generally, would be amply justified, and such an establishment was strongly recommended.

CHAPTER X.

The Control of Mosquitoes.

SECTION I.

In all the countries of the world where serious attempts to control mosquitoes have been made, a satisfactory measure of success has been gained only when it has been realized—often after much expenditure of time and money—that the task is everywhere one of great difficulty, needing all the resources and powers at the command of the Public Health Authority. This being so, it may be stated at once that it is futile to initiate an anti-mosquito campaign unless the arrangements from the beginning are those to which other countries have been brought by years of experience. For that reason it will be most useful to begin this account by noting some of the principles on which the arrangements for a modern campaign in a mosquito-infested municipality in the tropics are based:—

(1) In the early years of anti-mosquito work it was assumed that in general all species of mosquitoes have the same habits and mode of life, and that operations based on this assumption could be prosecuted without special inquiry; but it is now held, as a first principle, that anti-mosquito work upon which public money is to be expended must be preceded and accompanied by research, to ascertain at least:—

(*a*) The particular species that are dangerous in the area and those that are troublesome.

(*b*) The distribution, numerical prevalence, seasonal incidence, and the life history and habits of each of these species separately.

(*c*) The progress and results of the campaign.

Complete information collected under these headings is necessary in order to indicate, in the first place, what practical methods will be most likely to reduce the different species, and, in the second, to what extent the measures are successful when applied.

In order to carry this first rule into effect, it is usual to place the operations in charge of an officer who has received a thorough training in field entomology, and can devote his whole time to the campaign. He works in co-operation with the Medical Officer of Health, and, whenever necessary, receives assistance from the Engineering and Public Works Departments of the Municipality, and from the Military Authorities. He has under him one Sanitary Inspector, two or more Sub-

Inspectors, a Laboratory Assistant, ten or twelve Overseers, and a variable number of labourers. He trains all these men in the particular kind of work required.

(2) For some months, at least, the operations are confined to investigation, and in this connection it may be noted that, in studying the prevalence and distribution of the different species, methods for enumerating the adult insects, as well as the usual methods having reference to the prevalence of larvæ, should be devised and employed.

(3) The inquiry into the habits and mode of life of the different species will show how necessary it is to study each species separately. Possibly it will be found that the different species can be arranged as regards their habits into the five groups which were defined on p. 78. In any case it will be clear that the measures necessary for controlling some species (such as the household and other domestic species), must be quite different from those required for others (such as the swamp-breeding species). And it will now have to be decided *against what species* and *by what methods* the campaign shall be conducted.

(4) In connection with these decisions the following notes may be useful:—

(*a*) As a rule it is a wise policy to concentrate against one or two species only, rather than attempt to reduce all species in an area. This is because, at present, we do not know a better method of attacking mosquitoes than the endeavour to obliterate their breeding places; and this method is ineffective to the extent that, *until a high percentage of the total potential breeding places in an area have been eliminated, no appreciable reduction of mosquitoes results.* Therefore, when the means at command are limited, if the available effort is dispersed in an attack on the breeding places of all species, no reduction of any species may be apparent.

(*b*) The particular species to be attacked must often be decided by the knowledge that a certain species is a carrier of some disease in the area, or that another species is so troublesome as to be a pest. But, if one has a choice in the matter, it is useful to know that the species with highly specialized habits (especially as regards breeding places) are the easiest to reduce, and that for this reason much greater success has attended efforts to reduce the "domestic" species (Group 1 and 2), and especially the strictly household species, than has attended efforts against any other kinds of mosquitoes. For the domestic species, strictly local measures confined to the town itself, and including no large drainage operations, may suffice; but for the rural species (among which are the *anopheline* mosquitoes) extensive operations beyond the town, and large measures of drainage and "filling" will probably be required.

(*c*) Next, as regards the particular methods to be employed in the campaign, it is unfortunate that, in the present state of ignorance as to the best plan of attacking mosquitoes, we have to depend upon an endeavour to obliterate potential breeding places and to destroy larvæ. But this being so, it is important to decide, before commencing a campaign, whether the attempt to obliterate breeding places shall be authorized and backed up by the law, or whether reliance will be placed on voluntary action only. To carry out the first plan it would be necessary for the municipality to take powers to require that every collection of water in the town shall be "screened" or in some other way kept free from the possibility of being a breeding place, and that, as regards collections of water on private land, the duty of preventing them from being breeding places shall rest upon either the householder or the owner. These powers obtained, the municipality would set an example by dealing thoroughly with all breeding places that are under its own control, and afterwards (when a reasonable period had elapsed) it would send trained inspectors from house to house to report upon the condition of private water collections as to mosquito-proofing and as to the presence or absence of larvæ; and on these reports it would act as to the serving of notices, and, when necessary, fining the tenant or owner according as the responsibility might rest.

In the second or voluntary plan of campaign the municipality itself undertakes all the work necessary for the elimination and destruction of breeding places, the householders and owners of land assisting only in so far as they can be brought to do so by persuasion, instruction, and example.

As regards anti-mosquito work in the tropics, the arguments in favour of a plan of campaign authorized and backed up by the law greatly outweigh those in favour of a voluntary campaign; and in actual experience the former plan has been found to be necessary wherever anything more than a purely temporary success against the household and other domestic mosquitoes has been desired.

(5) When the investigation has proceeded to the stage at which the above decisions can be made, the most profitable policy is to institute experimental anit-mosquito measures in conjunction with the investigation, and so to continue until the best arrangements and methods for dealing with the different species, in the particular locality concerned are plain. These arrangements and methods can then be pushed with confidence, and perfected until the desired result is attained.

The experimental measures will be, of course, small in scope, and will be carried out in different parts of the town or district; they are to serve as samples of the methods to be employed, as a means of ascertaining what staff will be necessary for applying the methods throughout the town or district, and what will be the initial and recurring cost of the scheme as a whole. Their progress and results should be systematically tested by the following methods and such others as can be devised.

(*a*) A continuous record of the number of potential and actual breeding places found in the experimental area at each weekly inspection. The correctness of the record made by the staff allotted to a particular section of the area should be checked from time to time by means of "independent investigations" made by the staff of another section of the area.

(*b*) A periodical comparison of the number of actual breeding places found inside the experimental area with the numbers that can be found in a similar "control area" outside it.

Both the above methods of test relate to the presence of larvæ only; they measure the progress made towards extirpation of breeding places, but afford no test of the degree to which adult mosquitoes may or may not have been reduced. As regards tests of a lessened prevalence of adult mosquitoes, the following should be used:—

(*c*) The opinion of members of the community occupying the area dealt with as compared with the opinion of people living outside the area. This method is chiefly useful when mosquitoes are so numerous as to be described by most people as being a pest, or so rare as to be thought by most people to be absent.

(*d*) Enumeration by hand-catching in tubes.

(*e*) Enumeration by catching in special traps.

(*f*) The use of "test breeding places."

All these observations should be controlled, as far as possible, by observations made at the same time outside the experimental area.

(6) The particular methods at present available for destroying the adults, larvæ, and eggs of mosquitoes are described in Section II of this chapter, but a point of some importance and interest will not be out of place here. In the early years of anti-mosquito work it was thought that methods for destroying larvæ, and for eliminating possible breeding places, would comprise all the important methods of attack against these insects; but more recently it has come to be believed that other methods (and especially methods of a "constructive" kind) may ultimately prove more useful and effective. It often happens that the good effects of anti-larval operations in an area are nullified (*a*) by the flight, or infiltration, or importation, of adult mosquitoes from outside the area: (*b*) by the failure to reach the necessary degree of elimination of breeding places mentioned in paragraph 4 (*a*) above; (*c*) by the fact that, when all the obvious breeding places in an area have been obliterated, the adult insects seek less obvious and often quite inaccessible collections of water in which to lay their eggs. For these and other reasons practical workers are beginning to realize that the best hope of success against mosquitoes may lie in a more exact and intimate study of the habits of the male and female adults, and in methods of attacking the insect in that stage of its life. The proved efficacy of attractive traps for catching the adult insects and of "trap breeding places" is worthy of attention as a beginning in "constructive" methods, as is also the utilization of plans based on the knowledge that certain animals are more attractive to anophelines than is man.[1] And in connection

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[1] Observations made under natural conditions in the Isle of Grain seem to indicate that rabbits and pigs are particularly attractive to *A. maculipennis* in this country.

with the detection and destruction of adult mosquitoes even in England it is possible that more use might be made of the knowledge that cowsheds are a favourite resting-place of some anophelines. At any rate, we know enough to realize that it is often a mistake to make cowsheds unattractive to mosquitoes —for on certain occasions when this has been done the insects have sought shelter in the nearest dwelling house. It is known that certain scents repel mosquitoes, and experiments with other insects indicate that possibly there may be a substance or a method that will attract them. It is obvious that, if a substance with that property could be found, many of the problems which now present great difficulty and expense would be solved.

CHAPTER X (*continued*).

SECTION II.

METHODS AVAILABLE FOR DESTROYING THE ADULTS, LARVÆ AND EGGS OF MOSQUITOES.

MEASURES AGAINST THE ADULT INSECTS.

(*a*) *Methods for catching and killing.*

(1) *Hand-catching.*—In rooms, huts, tents, barracks, &c., the adult insect may be caught: (*a*) in dry test-tubes; (*b*) in test-tubes containing a few drops of chloroform on cotton wool; (*c*) in entomological hand nets.

This is the best method of freeing from mosquitoes the wards and bedrooms occupied by malaria patients. It should be employed systematically every day, especially in wards and rooms that have been "screened" or "mosquito-proofed," because mosquitoes often succeed in effecting entry into such rooms but rarely find an exit. In the screened barracks at Miraflores, on the Panama Canal, in April, 1912 (the dry season), the average daily catch made by four men working for two or three hours each day was sixty; but as many as 500 had been caught in one barracks at other seasons.

(2) *Cutting and removal of "jungle" and other vegetation* in which mosquitoes shelter.—Many species of mosquitoes spend the daytime hidden among long grass or in bushes and other coarse vegetation, and the removal, cutting, burning, or "tidying up" of such vegetation is one of the most efficient means of keeping houses free from these pests. On the Panama Canal this work was very thoroughly done by burning with "flame-throwers" (fig. 98) all grass and coarse vegetation in the vicinity of dwellings, and in India the removal of "jungle" is regarded as an anti-malarial measure of great importance.

FIG. 98.

(3) *Catching in traps.*—A suitable mosquito-trap was described and illustrated on p. 71. From experiments with these traps, I surmised that, if every householder in Colombo could be induced to use such a trap correctly, about ten million mosquitoes might be caught daily and that this would be more effective than the daily destruction of 1,000 million larvæ.

Similar traps consisting of dark cloth bags or black boxes can be usefully employed in houses; and specially designed traps fitted into the frame-work of screened houses have been found very useful in the tropics. In the screened hut shown in fig. 99 such a trap is fitted over the door and another in the side. This hut was used as an observation post during an experimental anti-mosquito campaign in Colombo in 1913.[1]

(4) *Fumigation.*—The fumes of burning sulphur are a satisfactory means of killing mosquitoes in cellars and outhouses where they "hibernate" during the winter, but the fumes damage metal ornaments and other household goods. The cellar must be closed as tightly as possible and paper must be pasted over all crevices. The iron pot containing the lumps of sulphur should be placed in a bucket on bricks in the centre of the room, and a few ounces of methylated spirit should be poured over the sulphur. After lighting the sulphur the room should be kept closed for two hours. The amount of sulphur required is two pounds for every 1,000 cubic feet of space.

FIG. 99.

(5) *Spraying.* — Adult mosquitoes in cellars, stables and outhouses can also be killed by spraying the walls, ceilings, rafters, &c., either with "Army Spray" (diluted 1 in 20 with water) or with a weak solution of formalin. All food and milk should be removed from the room before using these sprays.

(*b*) *Methods for driving Mosquitoes from Rooms, &c.*

(1) After opening all doors, windows and cupboards, thoroughly shake all bed hangings, curtains and clothes that are hanging up. Then with a long broom vigorously sweep the ceiling, walls, the tops and backs of wardrobes, bookcases and cupboards, and all dark corners. Dust the backs of all pictures, the tops of curtain poles and the undersides of all chairs and tables.

(2) Of the numerous fumigating agents which drive mosquitoes from rooms, but do not kill them, pyrethrum powder and cresol are probably most useful for general

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[1] See "Report on a Mosquito Survey of Colombo and the Practicability of reducing Stegomyia and some other kinds of Mosquitoes in that Seaport," Government Record Office, Colombo, 1914. Price 2 rupees.

use. About a tablespoonful of dry pyrethrum powder heaped into a pyramid and burnt from the top is sufficient for an ordinary room; and if cresol is used, heat about a tablespoonful in an iron pot over a gas-jet until it volatilises.

MEASURES AGAINST THE LARVAL STAGE.

The chief measures are:—

(1) To *abolish* collections of water that may be actual or potential breeding places.

(2) At least once a week to *empty and thoroughly dry* water-containing pools and household vessels.

(3) To *cover* collections of water in such a way that mosquitoes cannot lay their eggs in the water.

(4) To apply "*larvacides*" to collections of water.

(5 and 6) To apply *efficient drainage methods and* "*filling*" *operations.*

(7) To endeavour to *render permanent collections of water inimical to larvæ* by clearing out all vegetation and making the edges hard and smooth without any side pools or backwaters.

(8) To stock collections of water with *larvæ-eating fish.*

The following are notes on arrangements that may be necessary in connection with these measures.

(1) *Abolition of possible breeding places.*—An effective campaign for abolishing breeding places may require:—

(*a*) The introduction of a new or an improved water-supply system which will obviate water-storage in houses.

(*b*) The introduction of a better system for the collection and disposal of disused household receptacles and other articles which, not being required by the people, may collect rain-water, and harbour mosquito larvæ.

(*c*) The removal or repair of such roof gutters as do not automatically become empty after rain (B, fig. 100).

(*d*) The removal of trees containing rot-holes, or the filling of the holes with cement (A, fig. 100).

(*e*) The removal of water-holding plants of all kinds (C, fig. 100).

(*f*) Efficient systems of drainage, and extensive operations for filling depressed areas and lowering the level of the subsoil water.

(2) *Emptying Pools and Household Utensils.*—It is not sufficient only to empty pools and utensils; the larvæ and eggs which remain in the mud or inside the jars and other utensils must be killed by drying or other means (see p. 76).

(3) *Covering or* "*Screening.*"—The covers for making cisterns, wells, reservoirs, &c., mosquito proof, may be of any material that fits closely enough to prevent the entry

of mosquitoes. The outlets of the overflow pipes from cisterns, &c., should be provided with flap-valves. When wire mosquito-proof netting is used for covering collections of water its grade should be not less than 16 meshes to the inch, and preferably 18 meshes. Muslin should be used as a temporary expedient only.

(4) *Larvacides.*—These are :—

(*a*) Oils which, by forming a layer on the surface of the water, prevent the larvæ from obtaining air.

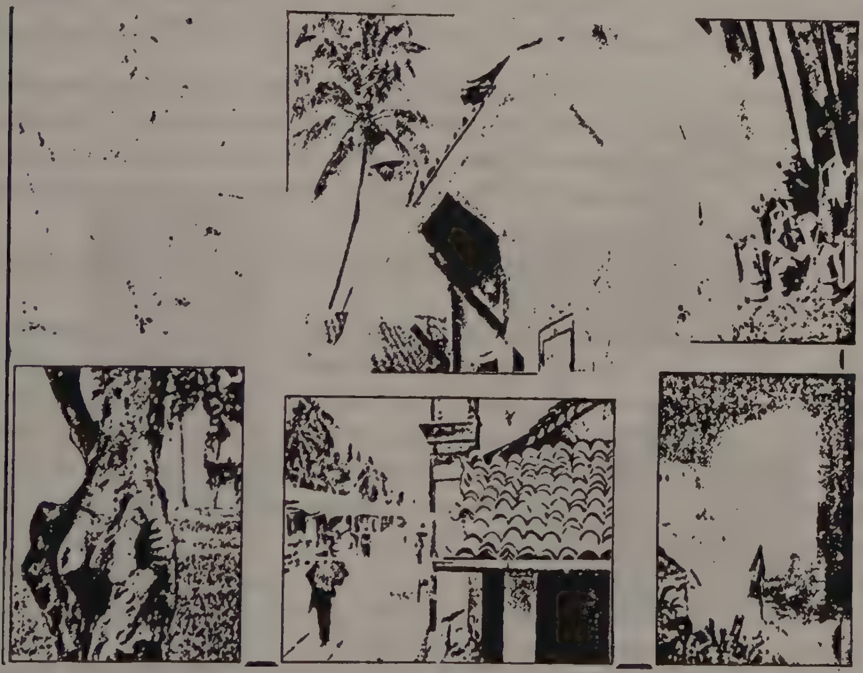

FIG. 100.—A, rot-holes in trees; B, roof gutters with blind ends where water lodges; C, cut bamboos and a common water-holding plant.

(*b*) Poisons which, when mixed with the water, kill the larvæ.

Mixtures of crude oil and kerosene oil are generally used to form a layer on the surface of water, the mixture being sprayed from a watering-can or a special apparatus. The treatment is efficacious only when the whole surface is covered with a complete unbroken layer. In practice this is difficult to ensure, and in extensive operations larvacides of the second class have been found to be more certain in action and more lasting in effect. Commercial cyllin is one of the most useful agents: one teaspoonful in a gallon of water kills larvæ in a few minutes and pupæ in less than thirty minutes. In practice it is a good rule to add enough cyllin to make the water remain quite milky after it has been well stirred with a stick.

The formula of the larvacide invented and used in the operations on the Panama Canal is :—

Resin	150 to 200 lbs.
Caustic soda	30 lbs.
Crude carbolic acid (containing not less than 15 per cent. phenol)	150 gallons.
Water	6 gallons.

The carbolic acid is heated in a tank fitted with steam coils. When steaming hot the powdered resin is added and dissolved by continuous stirring. The caustic soda is dissolved in six gallons of water and added to the resin-carbolic mixture. Heat and stirring are continued for five minutes or more until a sample emulsifies well on being added to water.

A 1 in 5,000 emulsion should kill anopheline larvæ in ten minutes. The larvacide fails in brackish water.

(5) *Drainage.*—The methods of drainage which are effective in controlling mosquitoes are for the most part of a special kind and cannot be described briefly. They are best learnt by practical experience in the field, but the following hints may be noted here. For some of them I am indebted especially to Dr. Orenstein who very kindly explained and demonstrated them to me during a visit to Panama in 1912. The best available account of anti-mosquito drainage methods is contained in the book entitled "Mosquito Control in Panama," by J. A. Le Prince and A. J. Orenstein.

(*a*) Schemes of drainage designed from the point of view of the agriculturist (who may wish to retain water underground) are not always best from the point of view of the malariologist (whose object may not be attained until the whole ground has been dried as much as is possible).

(*b*) The detailed plans for surface drainage should be devised during a rainy season, as it is only during such periods that the best arrangement of minor drains can be worked out.

(*c*) Important subjects to be considered in connection with the scheme are the arrangements for water-supply, for disposal of sewage, of sullage water and of storm water. In the East, the result of bringing a water-supply into a town from outside, without first providing for the efficient removal of all superfluous water, has often been to increase the waterlogging of the soil and to cause the formation of numerous pools where mosquitoes can breed.

(*d*) In carrying out the scheme the endeavour should be not to obtain immediate results by ill-considered and hurried works of an imperfect and temporary nature, but to carry out thoroughly each year such portions of the comprehensive scheme as the funds available allow.

(*e*) Open ditches in which the tide flows and ebbs are successfully used to control the mosquitoes that breed in the salt marshes of the American North Atlantic coast, but a similar system was only partially successful in Colon on the Panama Canal. On the North Atlantic marshes the system is planned so that the entire length of all ditches will be flushed by every tide. The ditches are dug by special machinery; they are about 200 feet or less apart, and from 10 to 24 inches wide and 30 inches deep, the sides being perpendicular. This type of ditch is shown in the abov illustration (fig. 101), which is from a circular entitled "The Mosquito must go," b Thomas J. Headlee, and Mitchel Carroll, issued by the New Jersey Agricultura Experiment Station, April, 1919. An illustration of the "power-ditcher" wit which this drain was cut is also reproduced from the same publication (fig. 102) The efficacy of the system is said to depend partly on the drying of the mars surface, which is normally about one foot above mean high tide, partly on the fac that the ditches let in the tide which, by completely covering the marshes, allow small fish which are voracious larva-eaters to penetrate into every small pool.

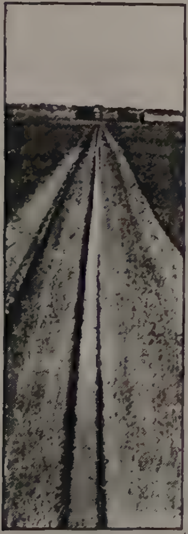

Fig. 101.

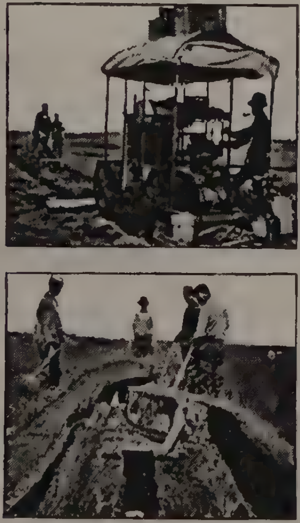

Fig. 102.

(*f*) Open earth ditches of similar character on flat marshy land (but without tidal inflow and outflow) and open contour ditches on hill slopes, were extensivel tried on the Panama Canal, but it was found that the sides often broke down and that the ditches became much clogged with vegetation, so that unless such drains can be regularly cleaned, *and systematically treated with larvacides,* they form dangerous breeding places. An illustration of some contour ditches of this kind on hill slopes is reproduced here (fig. 103) from a valuable article by C. W. Metz, in "The United States Public Health Reports," vol. xxxiv, No. 5, January 31, 1919.

(*g*) A great advance was the adoption of a system of shallow open cemented, plastered or "grouted" ditches, and this system is held to be the *correct* way of dealing with flat marshy land. It is also the best way to deal with the drainage of hill sides which have only a gentle slope. A "grouted" ditch is formed of a layer of hen-coop netting between two layers of concrete made with one part of cement and two parts of rubble. These ditches must have key walls about every 30 feet; and all cemented or plastered ditches must have "weep-holes" about every two feet, the weep-holes pointing upwards. The lining of the ditch should be smooth and rounded or oval. V-shaped cement ditches are expensive, and a special instrument is required for cleaning them out.

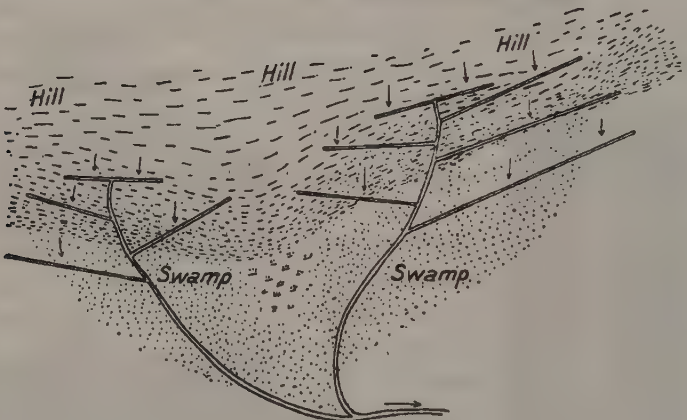

FIG. 103 (after Metz).

(*h*) Flat marshes may sometimes be satisfactorily dealt with by the special system called "Vertical Drainage." This means that holes or "wells" are bored vertically through the impervious layer of soil which is holding the water on the surface of the ground.

(*i*) Streamlets on slopes and hillsides, especially when among rocks or large stones, are often dangerous breeding places. They should be "trained" and carried in a smooth plastered channel. Much excellent work of this kind has been done in Hong-Kong. Subsoil drainage by tile pipes has sometimes been recommended for dealing with streamlets, but quite wrongly. If it is necessary to carry a streamlet underground this must be done in a properly constructed iron drain-pipe with manholes.

(*j*) So called "blind drains" are sometimes useful. They are made as follows: Dig a ditch and line the bottom and sides with large flat stones. Place cover-stones over these, and fill in with smaller stones to a height slightly above the level of the surrounding land.

(*k*) *Subsoil drainage* by means of unglazed tile pipes was at one time much praised as an economical and permanent method of abolishing breeding places in marshy districts, but those who have had most experience with the method now consider that it has only a limited application. It is—

FIG. 104 (after Headlee and Carroll).—Ditching spades and plough.

(i) Not applicable for flat land.

(ii) Not applicable for streamlets or any surface water: it should never be used with the object of catching water through the open ends of the tiles.

(iii) Not applicable where silt will get into the tiles.

The proper application of subsoil tile drainage is for catching the *seepage water* which oozes out on the sides of slopes and hills. This seepage water, when not dealt with, collects in tiny depressions and pockets on the surface of the ground, and forms numerous breeding places often quite hidden among grass and weed.

The manner of laying subsoil tiles for seepage water drainage is as follows:—

(i) Dig a trench true to grade at right angles to the slope of the hillside, and ascertain by trial when it is at the correct depth for drying the surface.

(ii) Line it true to grade with small stones.

(iii) Lay the tile pipes end to end at right angles to the slope of the hillside.

(iv) Cover them with small stones tightly fitted and pressed.

(v) Crown with crushed stone or rock slightly above the level of the surrounding land.

(6) *Filling Operations.*—These are not less important than drainage and in some localities in the tropics they have been carried out on a great scale with the aid of suction dredgers, steam shovels, and other machinery. In smaller works, where the material for filling can be selected, it should be as far as possible of a kind that is porous, such as small stones, gravel, or ashes.

(7) The margins of artificial ponds should be lined with cement. Vegetation overhanging the sides of ditches should be burnt away with flame-throwers.

(8) *Larvæ-eating Fish.*—Nearly all small fish such as "sticklebacks," "top-minnows," and "goldfish" feed voraciously upon mosquito larvæ; and artificial ponds and lakes, rice fields, &c., which cannot be more radically dealt with, should be stocked with them. It is important, however, to keep such ponds free from vegetation which shelters the larvæ from the fish.

MEASURES AGAINST THE EGGS.

The eggs of some species of mosquitoes are frequently to be found on damp mud instead of on actual water, and the eggs are able to withstand a considerable degree of drying. For example, the mud that remains in roof gutters frequently contains mosquito eggs which hatch out at the next rainfall. To prevent this it is usual to spray the mud with larvacide which will mix with the water and kill the larvæ. The muddy sides of partly dried streamlets are also sprayed with the same object.

OTHER MEASURES.

Trap Breeding Places.—It is unfortunately the case that when most of the obvious breeding places in an area have been eliminated, the adult insects seek less obvious and more inaccessible collections of water in which to lay their eggs. To circumvent this it is a good plan to place what are called "trap breeding places" in various parts of the area. These should be collections of water in vessels or artificial pools of the kind usually chosen by the particular species of mosquito that is being dealt with, and they should be examined (and the larvæ in them destroyed) every sixth day.

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ERRATA AND ADDENDA.

Page 22.—Leishman's stain. The amount of powder stated as 0·15 gramme should read 0·015 GRAMME.

Page 40.—In fig. 27 the word abium should read LABIUM.

Page 52.—English anophelines. Add the following to the publications mentioned: "A Handbook of British Mosquitoes," by W. D. Lang, M.A., Sc.D. Published in March, 1920, by the Trustees of the British Museum (Natural History), Cromwell Road, S.W. 7. In this book all the known species (twenty-one in number) of mosquitoes found in the British Islands are described and illustrated in a manner which enables them to be identified without difficulty.

Page 53.—Blacklock and Carter have shown that both *bifurcatus* and *plumbeus* can act as efficient hosts of *P. vivax* in laboratory experiments in England. See *Annals of Tropical Medicine and Parasitology*, vol. xiii, No. 2, pp. 31-7, 1919, and subsequent numbers. But in nature neither species has yet been found responsible for a new case in this country.

At Taranto (Italy) during 1918 both *bifurcatus* and *maculipennis* were found to be carrying malaria, but the latter more frequently. See "A Report on the Anti-malaria Campaign at Taranto during 1918," by Colonel J. C. Robertson, I.M.S., published in the "War Office Observations on Malaria" (H.M. Stationery Office, December, 1919, price 6s. net). This publication, edited by Colonel Sir Ronald Ross, Consultant in Malaria, War Office, contains other articles including a valuable Report on the excretion of quinine in urine, by M. Nierenstein, D.Sc., Ph.D.

Page 89.—During 1919, 101 new cases of malaria contracted in England were notified or discovered. This brings the total cases discovered since August 1917 to 426.

Pages 189 and 201.—A good example of the efficacy of quinine in preventing relapses, when employed with proper supervision, was provided in 1918 by Lieutenant-Colonel J. Dalrymple, R.A.M.C. See the "War Office Observations on Malaria," pp. 132.

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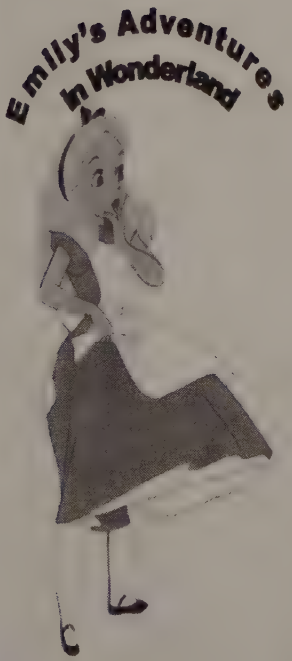

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